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Editorial

EL CARMEN DE BOLÍVAR: A LESSON NOT TO BE FORGOTTEN

The growing concern regarding the safety of vaccination against human papillomavirus (HPV) is no secret to anyone in Colombia. This concern arises from recent events in El Carmen de Bolívar a town located close to the north coast in the country, where more than 500 girls who were vaccinated presented a variety of symptoms that required medical care in the local hospital. The event reached such a magnitude that it not only overwhelmed the local health services in the township but also required the joint effort of several agencies of the national, department and regional levels to placate the irate population, restore law and order, and shed light on the facts (1).

Multiple theories have been proposed in an attempt to explain the sequence of events, but two of them in particular have been the focus of our attention: the symptoms reported may be explained as an adverse reaction to the vaccine, or as a somatoform disorder (mass psychogenic response). The objective of this editorial is to contribute to the current discussion by means of a critical assessment of the evidence regarding the safety of HPV vaccination and to approach the complexity of the problem that took place at El Carmen de Bolivar as a form of reflection on the issue.

To begin with, and in order to elucidate what happened, it is reasonable to ask "What are the adverse effects associated with the use of the HPV vaccine?" To answer this question, I will refer to the update of a systematic review of the literature published by the Instituto de Evaluación Tecnológica en Salud de Colombia (IETS) (Colombian Institute for Health Technology Assessment) (2), which identified two systematic reviews that analysed the safety of HPV vaccination (3, 4), rated as moderate quality using the Amstar tool (5) (score 8/11).

The first one (3) assessed the frequency of serious adverse events in women in the range of 15 to 45 years of age. The intervention consisted of the administration of the bivalent or tetravalent vaccine versus placebo or the hepatitis A or B vaccine. The outcome of interest was the frequency of any serious adverse events defined as the finding of any haematological or lymphatic, gastrointestinal, cardiovascular, muscle-skeletal or connective tissue, central nervous system, psychiatric, renal, reproductive or respiratory tract abnormality, or the development of any infection or neoplasm. The subjects were followed during 26 to 41 months, and adverse event reporting was done in writing within the first 15 to 30 days after the administration of the vaccine, and later during the six-month follow-up visits.

Based on this systematic review, it was determined that the administration of the HPV vaccine, compared with the control group, was not associated with a higher frequency of serious adverse events (RR = 1.00; 95% CI: 0.91-1.09; 7 studies, 43,856 participants, I^2: 0%). The quality of the evidence was considered moderate because some limitations associated with the risk of bias of the studies included. It is worth pointing to the accuracy of the results (narrow CI, optimal information size), the consistency among the studies (low heterogeneity), and the

applicability of the information (two of the studies recruited Colombian population) in the absence of publication bias.

On the other hand, the second systematic review (4) analysed the frequency of local or systemic adverse events following vaccine administration. The population included non-pregnant women between the ages of 9 and 45 years. Again, the intervention of interest was the use of the bivalent or tetravalent vaccine, compared with the use of placebo or the hepatitis A or B vaccine. This time, the outcome of interest was the frequency of any adverse event that could be classified as local (any degree of puncture site pain, erythema or oedema) or systemic (fever, fatigue, headache, myalgia or arthralgia). The subjects were followed for 7 to 48 months and adverse event reports were registered from the moment the vaccine was administered and then during every follow-up visit.

Based on this review, it was determined that the HPV vaccine is associated with a higher frequency of local or systemic adverse events such as pain (OR = 3.29; 95%: 3.00 to 3.60; 6 studies, 9,427 participants. I^2: 19 %); erythema (OR = 2.41; 95% CI: 2.17 to 2.68; 5 studies, 9,133 participants. I^2: 70 %); oedema (OR = 3.14; 95% CI: 2.79 to 3.53; 5 studies, 9,133 participants. I^2: 78 %); fever (OR = 1.21; 95% CI: 1.03 to 1.42; 4 studies, 8,788 participants. I^2: 0 %); fatigue (OR = 1.29; 95% CI: 1.18 to 1.42; 5 studies, 9,082 participants. I^2: 56 %); headache (OR = 1.17; 95% CI: 1.06 to 1.28; 4 studies, 8,788 participants. I^2: 61 %); myalgia (OR = 1.97; 95% CI: 1.77 to 2.20; 4 studies, 8,013 participants. I^2: 57 %); and arthralgia (OR = 1.40; 95% CI: 1.20 to 1.64; 3 studies, 7,719 participants. I^2: 40 %). The quality of the evidence was low because some limitations related to the risk of bias, inconsistency among the studies, and the inaccuracy of the results. This systematic review did not report serious adverse events.

Consequently, based on the available evidence, it may be concluded that, compared to the control group, the HPV vaccine appears not to increase the frequency of serious adverse effects (3), although it does increase minor local and systemic adverse effects (4).

Now, in terms of the hypothesis of a mass psychogenic response, after reviewing some articles, the situation of El Carmen de Bolivar is not very different. To start with, it is relevant to refer to the definition of a mass psychogenic illness as a set of symptoms suggestive of an organic disease of unclear origin, accompanied with little or no evidence of a disease that can be documented by diagnostic tests (6). The prevalence of this entity is unknown, but it has been reported around the world, involving people with *real symptoms* frequently triggered by wrong or misinterpreted information (7).

This disorder primarily affects females during childhood and adolescence typically in the form of a sudden, rapidly progressing clinical picture, with a short transmission pattern characterized additionally by the fact that other people potentially exposed do not fall ill (6, 7). Symptoms are usually preceded by environmental or community exposure (smell, rumour, reported toxin) (8) and consist typically of headache, dizziness, abdominal pain, fatigue, breathlessness, paralysis of one or several extremities, anxiety, and even loss of consciousness (7-9).

Unfortunately, by the time the outbreak was taken hold and the entity has been recognized, the event has already created a devastating effect not only on the affected individuals but the community in general (10). Regardless of the triggering factor, early recognition of this disorder is key and management requires a complex therapeutic approach; efforts must focus on reducing the impact on the exposed population (6).

In order to overcome the situation and ultimately resolve it, affected communities need to minimize their exposure to potential anxiety triggers (media coverage), must be advised promptly about the results of the tests performed, and must be given clear and truthful information that can help put and end to rumours or "suspicious causes" by means of constant and fluent dialogue with healthcare professionals (6, 8, 10).

Based on the above, it is not difficult to understand the event. Unresolved concerns of both parents as well as patients regarding the safety of the vaccine triggered the whole sequence of events. The lack of education and adequate communication, and the absence of an open discussion regarding the risks and benefits of the vaccine (11), created an unsurmountable barrier at El Carmen de Bolívar (12, 13), leading to rejection of the vaccine.

The events at El Carmen de Bolívar prompted us to remind ourselves that if we are to have a positive impact on health conditions, we cannot just rely on safe and effective measures (14), but we need also to educate patients and families regarding the benefits and risks of our interventions (11).

It is our duty to enable and promote informed decision-making, which means deciding together with our patients and not on their behalf. Perhaps this will be the only way to avoid future setbacks and to increase acceptance of effective healthcare interventions (11, 12).

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