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Review

Vaccination strategies in pediatric inflammatory bowel disease

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ABSTRACT

The incidence of pediatric inflammatory bowel disease (IBD) is rising, as is the use of immunomodulatory and biological drugs. IBD patients are vulnerable to infections owing to disease-related immunological alterations and drug-induced systemic immunosuppression. Although many infections are vaccine-preventable, vaccination coverage in IBD patients is insufficient. Current guidelines recommend that children with IBD follow the same routine immunization schedule as healthy children, avoiding live vaccines during immunosuppressive therapy. Immunization status should be checked at diagnosis, and patients should be immunized with the vaccines they need. Some studies have demonstrated a suboptimal immune response to vaccinations in IBD patients, but responsible mechanisms are poorly understood. In this manuscript, we provide a broad review of available data about vaccine coverage rates, immunogenicity and safety of both killed and live attenuated vaccinations in the pediatric IBD population; furthermore, we provide comprehensive information regarding current guidelines for immunization of children with IBD and their household contacts. A comprehensive search of published literature using the PubMed (http:// www.ncbi.nlm.nih.gov/pubmed/) database was carried out to identify all articles published in English from 1998 to March 2017, using the following key terms: "inflammatory bowel disease", "vaccination", "immunization", "immunogenicity", "safety" and "children".

Contents

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1. Introduction

Inflammatory bowel diseases (IBDs), encompassing Crohn's disease (CD), ulcerative colitis (UC) and indeterminate colitis (IC), continue to rise in incidence and prevalence worldwide, both in the adult and pediatric populations [1]. IBDs are defined as multifactorial disorders characterized by chronic relapsing intestinal inflammation, with a peak onset during adolescence and young adulthood [2]. Treatment during the last decade has been based on immunomodulatory and biological drugs, such as anti-tumor necrosis factor alpha (TNF-α), that are being used increasingly often and earlier during the course of the disease [3,4]. Clinical studies, registries, and case series have highlighted the increased risk of infection, notably opportunistic infections, in young and adult patients with IBD [5–7]. An opportunistic infection is defined as a serious, often progressive infection, caused by microorganisms that have limited virulence, but can cause serious disease related to a predisposing pathologic condition or its treatment [8]. The challenges are not only in managing these diseases, but also in recognizing, preventing and managing infections. Prevention of infections is a major issue for public health, and vaccination has shown to be one of the most successful strategies against the spread of several infectious diseases [9]. Accordingly, the European Crohn's and Colitis Organization (ECCO) recommends protection with vaccines for young and adult IBD patients, where appropriate and available [6]. In the present manuscript, we provide an upgraded review of literature regarding vaccination rates, immunogenicity and safety, and current guidelines for vaccination in children with IBD. To accomplish this, a comprehensive search of published literature using the PubMed MEDLINE database (1998–March 2017) was performed. The key terms "inflammatory bowel disease", "vaccination", "immunization", "immunogenicity", "safety" and "children" were used.

2. Immunization rate

The most efficacious way to minimize vaccine-preventable infections is through vaccinations. A complete vaccination schedule is important in pediatric patients with IBD, who are at a higher risk of infection and severe or fatal complications than the general population [10]. Nonetheless, vaccination coverage in IBD adult and young patients is reported as below that of healthy children [10,11]. Incomplete childhood immunization can be distinguished as IBD-related or non IBD-related [12]. IBD-related reasons include use of immunosuppressive drugs and disease flare at the time of scheduled immunization, while non IBD-related reasons include parental refusal, lack of awareness of routine immunization, recent move from elsewhere with different immunization schedules, needle phobia. Many studies have demonstrated that both gastroenterologists and patients underuse the tool of vaccination in patients with IBD [10]. Primary care practitioners and gastroenterologists are often unaware of any existing recommendations, resulting in the lack of appropriate counseling [13,14]. Patients are frequently worried about vaccine-associated complications or low effectiveness, finally resulting in unsatisfying adherence to vaccination programs and seroprotection [15,16]. A survey of 36 IBD patients [11] has reported on provided reasons for the refusal of a recommended vaccination, which included the supposed unnecessity of vaccinating (52%), the fear of possible vaccine-related side effects or adverse reactions (25%), doubts about effectiveness (14%), the high cost of the vaccine (6%) and discouragement from medical care providers (37%). Another survey of pediatric gastroenterologists [17] concluded that the main barriers to vaccination are the lack of coordination of care with primary care practitioners (even if only 28% believed that primary care practitioners were solely responsible for immunizations), poor access to immunization records, and the inability to offer vaccinations in their immediate area, thereby being obliged to refer patients to overburdened public health clinics for vaccines, which are often located far from their offices or in other cities. In a recent prospective cohort study carried out over 2 successive influenza seasons, educational intervention and providing of influenza vaccine during clinic visits has been associated with improved influenza vaccination rates [18].

3. Immunization strategies

In 2013, the Infectious Disease Society of America published a "Clinical Practice Guideline for Vaccination of the Immunocompromised Host", an evidence-based guideline for vaccination of immunocompromised adults and children [19]. They recommended vaccinating all IBD patients, following the same routine immunization schedule as in healthy children. Live vaccines can be used before the start of immunosuppressive therapy—at least 4 weeks before starting treatment in the case of the varicella vaccine, and 6 weeks before treatment begins in the case of the measles, mumps, and rubella (MMR) vaccine. In pediatrics, exclusive enteral nutrition is considered a valuable alternative for induction therapy and could therefore be used as a window allowing time to update vaccinations prior to prescribing immunosuppressive drugs [6]. If immunosuppressive therapy has already begun, guidelines recommend administering live vaccines after discontinuation for at least 3 months (only 1 month if corticosteroid monotherapy is being used). Fortunately, most children with IBD have already received live vaccines by the time of diagnosis, as live vaccines are routinely administered to young children, and IBD onset is less common in children younger than 5 years of age. Household contacts can safely receive inactivated vaccinations, as well as the MMR vaccine, without fear of harming or spreading the virus to the patient [20]. The varicella vaccine is also viable; if a vaccine-related rash develops and the patient is not immunized, it is enough to avoid close contact. Such a scenario does not indicate administration of varicella zoster immunoglobulin, as the secondary infection from the vaccine is expected to be mild [20].

The "cocoon strategy" refers to protecting vulnerable patients from infection due to close contact with those who have been vaccinated. Recently, a study investigated the "cocooning strategy" among patients with IBD for the first time, concluding that it is not sufficient to protect IBD patients [11].

3.1. Checking immunization status: how and when

The immunization status of the patient should ideally be checked at the time of IBD diagnosis, especially if there is no clear history of vaccination or wild-type infection [10]. According to the second ECCO Consensus (2014) on opportunistic infections in adult

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