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Immunization in patients with inflammatory rheumatic diseases

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Immunization represents the most efficient and simplest intervention to prevent certain viral and bacterial infections in the general population as well as in the vulnerable population of patients with inflammatory rheumatic diseases treated with immunosuppressives. Here, we present an updated review of literature data regarding the safety and efficacy of immunizations against different pathogens in rheumatic patients treated with conventional immunosuppressives or the newer biologic agents while at the same time we provide practical guidance for the appropriate vaccine administration in this patient population.

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Introduction

Infections remain one of the most common co-morbidities in patients with inflammatory rheumatic diseases regardless of the use of immunosuppressive therapies. Although most of the infections in these patients are mild, serious infections leading to hospitalization can occur and are usually due to common bacterial or viral pathogens that could be prevented by appropriate prophylactic vaccination. The efficacy and safety of vaccinations in patients with inflammatory rheumatic diseases has been the focus of many studies over the last two decades.

Here, we review the literature concerning the risk of various vaccine-preventable infections in patients with inflammatory rheumatic diseases as well as the efficacy and safety of vaccination in these patient populations. The effect of corticosteroids, conventional synthetic (cs-) and biologic (b-) disease modifying anti-rheumatic drugs (DMARDs) in vaccine efficacy is also discussed in detail.

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Infection risk in patients with inflammatory rheumatic diseases

There is much data available regarding the risk of contracting serious infections in patients having inflammatory rheumatic diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and systemic vasculitides. RA patients have been found to carry a 2-fold higher risk for hospitalized infections than the general population [1], whereas in a recent RA cohort, 40% received at least one course of antibiotics during the previous year [2]. The respective relative risk for hospitalized infections in patients with SLE has steadily increased over the last 20 years, exceeding 12-fold in 2011 [3]. Similar findings have been reported in systemic vasculitides [4]. A recent study showed that almost a quarter of patients with anti-neutrophil cytoplasmic antibodies (ANCA) associated vasculitides (AAV) developed a serious infection, with a 4-fold increase in mortality rate during a 3-year follow-up period [4]. Moreover, giant cell arteritis (GCA) patients carry a 2-fold increased risk for severe infections during the first year after diagnosis, with infections accounting for a third of all deaths [5].

Vaccination rates and reasons for non-vaccination in rheumatic patients

Despite the overwhelming literature and respective guidelines from various scientific organizations supporting immunizations in rheumatic patients [6–8], several studies have indicated that the vaccine coverage remains suboptimal in this patient population.

In a recent multicenter, international, cross-sectional study of RA patients (COMorbidities in Rheumatoid Arthritis-COMORA), the vaccine coverage against influenza and *Streptococcus pneumoniae* was found to be only 25% and 17%, respectively [9]. Multivariate analysis revealed that age, low disease activity, higher educational level, treatment with biologics, non-treatment with corticosteroids, and the presence of co-morbidities were independent factors that determined vaccine administration [9]. In a study of similar design (Assessment in SpondyloArthritis International Society ASAS-COMOSPA study) for patients with spondyloarthropathies (SpA), the rates for influenza and pneumococcal vaccination were 38% and 17%, respectively [10].

One study showed that even in countries with acceptable vaccination coverage, such as the UK, although 80% of RA patients had been administered influenza vaccine during their lifetime, only one-third of the patients received regular annual immunization (35%) [11]. In another recent UK study, the high influenza vaccine uptake in patients with RA was confirmed, although the respective rate for pneumococcal vaccination was only 44% [2]. Vaccinated patients had a 79% higher probability of suffering from a comorbidity and a 69% probability of being treated with biologics.

Several studies have explored the main reasons for non-adherence to recommended vaccination schedules in rheumatic patients. In a French study of 137 patients with different rheumatic diseases, the absence of recommendation by the treating physician was the leading reason for non-vaccination against influenza (58%), followed by the fear of adverse events (35%) [12]. Similar findings were reported by Hua et al. in a cohort of RA and SpA patients, where 79% of non-vaccinated patients against pneumococcus and 48%–61% against influenza never received such recommendation by their treating physician [13].

These findings indicate that the proper training of rheumatologists and general practitioners is a legitimate target for vaccination campaigns. This has been the focus of recent studies conducted in children and adults, which showed that simple strategies can increase vaccination rates in both adults [14] and children [15] with rheumatic diseases. In a study of 3717 rheumatic patients (66% with RA) by Desai et al., a simple intervention (point of care reminder form) applied to patients not up-to-date with pneumococcal vaccination increased vaccination rates from 67.6% to 80% in 1 year [14]. Vaccination rates did not change in the non-intervention group (52.3%–52%). Factors associated with vaccination included the described intervention, diabetes, age 56–65 years, and care from a rheumatologist with <10 years in practice [14].

Similarly, Harris et al. studied the impact of various interventions such as presentations to rheumatologists, creation of vaccination algorithms, pre-visit planning, and hard-copy and electronic reminders to providers on pneumococcal vaccination coverage in a cohort of 299 pediatric rheumatic patients [15]. They reported that conjugate vaccine coverage increased from 6.7% to 48.4% and polysaccharide vaccine coverage from 8.9% to 28.4%, whereas coverage for both vaccines increased from 0% to 23.2% 1 year after the intervention period [15].

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