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Topical Review

Vaccination in adults with autoimmune inflammatory rheumatic diseases

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ABSTRACT

There is an increased risk of infections in patients with autoimmune inflammatory rheumatic diseases (AIRDs). The risk is more due to immune dysfunction and increased use of immunosuppressive drugs (mainly with the introduction of biologicals). Some of these are vaccine-preventable infections. In this narrative review we have appraised the recent literature on vaccinations in AIRDs along with relevant recommendations available in India.

1. Introduction

The number of individuals with autoimmune inflammatory rheumatic diseases (AIRDs) being treated with immunosuppressive drugs is steadily increasing, mainly with the advent of biological disease modifying agents.[1] The risk of infections is also more in these groups of patients and vaccination is an effective strategy for prevention.[1] We did not have enough data from India[1]; but in the COMORA (international, cross-sectional) study, of 3920 enrolled rheumatoid arthritis (RA) patients only 25.3% had a vaccination for influenza, 17.2% had pneumococcal vaccination and only 10.3% had both.[2]

So, what is the need for vaccinating patients with AIRDs? Are they at increased risk of vaccine-preventable infections? Then what are the vaccine-preventable infections? What is the immunogenicity, efficacy and safety of these vaccines? These are some of the questions we shall try to address in this narrative review. A literature search was performed in Pubmed and Scopus from January 2015 to February 2016. Only articles in English and data of patients older than 16 years were included.

2. Infection in AIRDs

There is an increased risk of infections in AIRDs due to dysfunction of the immune system secondary to disease, use of immunosuppressive drugs and comorbidities.[3] In comparison to the general population, there is 1.7 times higher risk of acquiring an infection and 1.8 times higher risk of acquiring an infection necessitating hospitalisation.[4] Some of the drugs like TNFi (tumour necrosis factor inhibitors) with glucocorticoids in RA and moderate doses of glucocorticoids in systemic lupus

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erythematosus (SLE) increase the risk of infection. The rate of serious infections is more with biologics compared to synthetic disease modifying agents and 5 times more in SLE compared to RA.[5] The increased rate of hospitalisation in AIRDs is for pneumonia and the common causative organisms like influenza, streptococcus pneumonia and hemophilus influenza b (Hib) are vaccine preventable infections.[6] There is an increased risk of herpes zoster infection in patients with AIRDs.[6] The rate of herpes zoster infection had increased with advent of biologicals and is significantly higher with usage of Tofacitinib.[7] Human papilloma virus (HPV) infections are more prevalent in SLE patients due to defective clearance of the virus. Hence, the diagnosis of SLE itself increases the risk of developing cervical dysplasias and pre-malignant lesions. But surprisingly the prevalence of cervical cancer was not increased except for one study.[8]

3. Inactivated vaccines

The administration of inactivated vaccines in patients with AIRDs on immunosuppressive drugs is safe, but efficacy might decrease depending on the type of drugs. The ideal time of vaccination is before the start of immunosuppressive therapy and during stable disease.[3,4]

3.1. *Influenza vaccine*

The exact incidence of influenza in AIRDs is unknown, but the morbidity and mortality due to the same are increased.[3,6] The limited studies assessing the clinical outcome in vaccinated patients found reduced admission and mortality from influenza pneumonia. There is a strong recommendation for annual administration of (both seasonal and pandemic swine flu) influenza vaccine.[3] In patients with RA, rituximab and abatacept reduce the antibody response significantly.[6] In SLE patients the vaccine efficacy is reduced with high disease activity, lymphopenia and therapy with azathioprine.[3,6]

3.2. *Pneumococcal vaccine*

The risk of invasive pneumococcal infections is more in patients with AIRDs. The risk is higher in patients with inflammatory arthritis on TNF inhibitors. The risk is also more in patients with SLE, scleroderma and sjogren syndrome.[3,6] Most of the studies on vaccination measure the serological response rather than the clinical outcome or endpoints.[4] Pneumococcal polysaccharide vaccine (PPSV 23) was found to be safe and effective in terms of serological response. Prolonged use of high-dose steroids was associated with poor vaccine response and increased rate of infections.[9]

In a study by Nagel et al., the efficacy of pneumococcal conjugate vaccine (PCV 7) was assessed in patients with chronic RA and spondyloarthritis (SpA). They found that the patients with robust serological response had less likelihood of developing serious infections. Similar to the previous study, high-dose glucocorticoids and older age were associated with serious infections.[10] Rituximab[4,6] and abatacept[11] causes a significant reduction in immunogenicity. MTX with or without TNFi[4,6] reduces efficacy to some extent. There are two types of pneumococcal vaccine (PPSV 23 and PCV 13) available, and as per the recent recommendations of the Advisory Committee on Immunization Practices (ACIP) the conjugate vaccine (PCV 13) is preferred over polysaccharide vaccine (PPSV 23).[12,13] The ideal approach would be to give conjugate vaccine first and follow it up with polysaccharide vaccine (prime and boost strategy). The conjugate vaccines induce higher affinity antibodies with long-lasting immune and memory responses.[4,13]

3.3. *Human papilloma virus vaccine (HPV)*

Three types of HPV vaccine (bivalent HPV vaccine [2vHPV], quadrivalent [4vHPV] and 9-valent vaccine [9vHPV]) are available. All the 3 types can be used in females but only the 4vHPV and 9vHPV in males.[12] This is indicated in few high-risk groups, like SLE patients. They have increased risk of HPV infections with a 9-fold increased risk of pre-malignant cervical lesions.[8] There is increased reporting of venous thromboembolism events with the 4vHPV type. Hence, extra caution is needed in SLE patients with anti-phospholipid antibody syndrome.[14]

3.4. *Others*

Tetanus toxoid vaccination is efficacious in RA patients on synthetic or biological DMARDS (including rituximab).[6] But in high-risk cases, it is safer to administer passive immunisation, if the patient had received rituximab in the last 6 months.[14] In SLE patients, active disease and steroids might decrease the vaccine efficacy.[4]

Both Hepatitis B and Hepatitis A vaccines are recommended in high-risk groups (i.v. drug abusers, health care personnel, multiple sex partners, etc.).[12,14] Hepatitis B vaccine had a satisfactory immune response in all rheumatic diseases and with all drugs except TNFi, which severely hampers the immune response.[4] The Hepatitis B and Hepatitis A vaccines are safe and immunogenic. But, there have been case reports of worsening of autoimmune diseases with Hepatitis B vaccine.[3] In AIRD patients with splenectomy or functional hyposplenism, vaccines against capsulated organisms like H. influenzae, meningococcus, including pneumococcus need to be considered, as per ACIP recommendations.[12,14]

4. Live vaccines

In general, live vaccines should be avoided in patients on immunosuppressive drugs and to be given prior to initiation of treatment. The reason is due to risk of replication of the attenuated microorganism. Some vaccines have a high-risk of replication (e.g. yellow fever vaccine) and some have a low risk of replication (e.g. herpes zoster vaccine).[3]

There is an increased risk of herpes zoster in patients with RA, SLE and granulomatous polyangitis (with renal dysfunction). The risk also increases with the use of cyclophosphamide and steroids with or without DMARDs/TNFi.[6] In two of the large retrospective cohort studies, herpes zoster vaccine was found to be safe and immunogenic.[4] Similarly, Measles–mumps–rubella (MMR) revaccination was found to be safe and