Complications of Treatments for Pediatric Rheumatic Diseases

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KEYWORDS

• Pediatric rheumatic disease • Treatment • Complications • Side effects • Infections • Immunizations • Childhood lupus • Juvenile idiopathic arthritis

KEY POINTS

- Biologic response modifiers (BRMs), which target specific mediators or cells involved in immunity and inflammation, have improved outcomes in childhood rheumatic diseases; they may be used in combination with nonsteroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs, or glucocorticosteroids.
- Physicians caring for children with rheumatic disease should be aware of possible toxic, metabolic, neoplastic, and infectious side effects of these different medications.
- Children on antirheumatic treatment are susceptible to unusual and opportunistic infections, and usual childhood infections, for which they should receive the usual immunizations with non-live vaccines.
- Medical care providers should consult with the rheumatologist immediately for potentially serious illness, which could represent a complication of treatment, disease flare, or both.

INTRODUCTION

The medications typically prescribed to treat various childhood rheumatic diseases have been discussed in previous articles in this issue. As a group, these medications are associated with risks for noninfectious and infectious side effects. Naturally, parents and patients worry about the possible side effects of medications[1] but do not always sufficiently appreciate the entire spectrum and severity of consequences of undertreated or untreated rheumatic disease. Nor do they always appreciate that, despite possible side effects, most medications prescribed for childhood rheumatic disease by pediatric rheumatologists have an acceptable to excellent benefit/risk ratio. Primary care providers (PCPs) are often consulted about the advisability of taking medications recommended by subspecialists. Along with emergency physicians and hospitalists, the PCP may be the first medical care provider who sees the rheumatic

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disease patient with a possible medication side effect. These providers are likely not well acquainted with all risk factors and potential toxicities associated with disease and medications. This article provides an easy-to-read reference on these morbidities. It consists of three parts:

1. First there is a general discussion of possible medication side effects and the potential difficulties in assignment of causality in individual children with rheumatic diseases.
2. The second section discusses potential side effects of medications individually and is organized by category of medications rather than by disease. This arrangement was chosen because the same medications may be used for treatment of more than one disease, and potential side effects are generally similar among children irrespective of their specific rheumatic disease. In this section, toxic/metabolic and infection-related side effects are discussed.
3. Finally, of special interest to the PCP, individual immunizations are discussed relative to contraindications, timing, and likelihood of protective response.

MEDICATION SIDE EFFECTS

Association Versus Causality

Large population studies can measure the incidence of various signs and symptoms in patients who take a medication versus those who do not. However, it can be difficult to determine the cause of a new symptom in an individual child or adolescent with rheumatic disease, particularly if it is a common symptom, such as rash, abdominal discomfort, headache, or behavioral change. There may be little information available to decide if the symptom is a new manifestation of the disease itself, a treatment side effect, or something unrelated. In the labeling information for medications, the designation of certain signs and symptoms as "associated" speaks to the difficulty of assigning causality. In an individual patient, sometimes a careful interval history can tease out the cause. Other times, it may be safe to stop a medication and later restart it to demonstrate correlation with signs and symptoms, providing evidence of causality.

Degree and Type of Risks

It is important to understand that for any one patient, the absolute risk of any adverse event caused by any medication can be difficult to determine. Type and degree of risk are related not only to the mechanism of action of an individual drug but also to medication dose and duration, concomitant use of other medications or substances, the disease for which it is given, age, lifestyle, and hereditary factors. Side effects of medications used to treat rheumatic diseases can be generally divided into metabolic, toxic, neoplastic, and infectious. The metabolic adverse effects include conditions like weight gain, fatigue, and decreased bone density. Toxic side effects result in injury to tissues and organs (eg, skin, liver, kidney). These types of side effects are more common with older, less specific treatments, such as nonsteroidal anti-inflammatory drugs (NSAIDs), glucocorticosteroids (GCS), and nonbiologic disease-modifying antirheumatic drugs (DMARDs). Infection is almost never a side effect of NSAIDS, but is of concern, to varying degrees, with GCS, DMARDSs and biologic response modifiers (BRMs). Neoplasms have also been associated with DMARDs and BRMs. The categories of neoplastic and infectious risks are discussed in more detail next.

More about risk for neoplasms

Because immunosuppressive medications can interfere with immune surveillance, neoplasms are on the list of possible side effects of some medications used for