Summary

- Timing of medication in relation to mealtime influences absorption and bioavailability of drugs.
- Fish-oil supplementation can reduce prostaglandin production and proinflammatory cytokines. Nonsteroidal anti-inflammatory drug use can be modulated by fish-oil supplements.
- Folate status is important for prevention of methotrexate toxicity.
- Side effects of medication, pathological process of the disease, low appetite, and low mobility from active disease can contribute to poor nutritional status of patients with rheumatic disease.
- Optimal nutritional status should be maintained to achieve a positive treatment outcome and to reduce the risk for developing concurrent diseases.

Key Words: Antioxidant; fish oil; folate; methotrexate; nonsteroidal anti-inflammatory drugs; proinflammatory cytokines; prostaglandin E₂

1. INTRODUCTION

Rheumatic diseases include more than 100 diseases that are characterized by inflammation, pain, and degeneration of connective tissues and joints. Treatment plans for rheumatic diseases vary depending on the type of disease and the patient’s condition. Medications for the treatment of rheumatic diseases are often used to relieve symptoms and prevent further worsening of the disease rather than to cure the disease. Lyme disease, infectious arthritis, and gout are some of the exceptions in which case symptoms of arthritis can be prevented or cured with early intervention and proper medications.

Drug–nutrient interactions can change both the therapeutic efficacy of medications and the nutritional requirements of patients. Therefore, understanding potential drug– and food– or nutrient interactions is crucial for maximizing biological effectiveness and minimizing the side effects of medications while ensuring optimal nutritional status of patients.

Medications most commonly used for the treatment of rheumatic diseases are nonsteroidal anti-inflammatory drugs (NSAIDs) to control pain and inflammation, corticosteroids to decrease inflammation and suppress the immune system, and disease-modifying anti-rheumatic drugs (DMARDs) to slow or prevent the damage to the
joint. Anticytokine-based therapies have emerged recently and are often used in combination with conventional therapies. Potential drug–nutrient interactions are reviewed in relation to these different categories of therapies.

2. MECHANISMS OF DRUG–NUTRIENT INTERACTIONS

There are several mechanisms by which drug–nutrient interactions may result in altered therapeutic efficacy of drugs or altered nutrient requirements of patients.

2.1. Alteration of Pharmacokinetics by Food

Foods may interfere with or alter the absorption or metabolism of drugs and cause a change in pharmacokinetics (1). Food can affect drug absorption and bioavailability by its effect on gastrointestinal (GI) physiology, including gastric emptying, acid secretion, intestinal motility, and bile secretion; and by physicochemical interactions between the drug and food components in the gut lumen and competitive inhibition between the drug and food components for absorption. Physicochemical interactions between nutrients and drug components include adsorption, complex formation, precipitation, and change in stability. Physicochemical interaction requires the simultaneous presence of the drug and the food component at the site of interaction. Therefore, timing of medication use in relation to food intake can influence the absorption of the drug. Additionally, the potential for a food–drug interaction is dependent on the region of the GI tract where the drug is absorbed. Drugs absorbed only in the upper intestine have a greater potential for reduced absorption when given with food (2). Certain rheumatic disease medications such as methotrexate and penicillamine should be taken in a fasting state to prevent a decrease in absorption (1).

2.2. Modulation of Biological Mediators of Rheumatic Diseases by Nutrients

Nutrients can modulate the course of therapy by their effects on biological mediators of rheumatic diseases such as cytokines and prostaglandins. Nutrients may have their own effect on the symptoms associated with rheumatic diseases, and as such, may influence the dose requirements of drugs. Nutrients may also affect side effects of the drugs to make the medication more or less tolerable. Omega-3 (n-3) fatty acids have been shown to have a significant impact on the production of eicosanoids and proinflammatory cytokines, which play a crucial role in the pathology of rheumatic diseases (3).

2.3. Change in Nutritional Status by Drugs

Drugs can often change the nutrient status of the patient. Certain drugs have a direct antagonistic effect on a specific nutrient. Methotrexate is a well-known folate antagonist (4). Drugs can also cause low levels of certain nutrients by interfering with nutrient absorption. Corticosteroids for the treatment of rheumatoid arthritis (RA) may impair intestinal calcium absorption (5). Therefore, dietary intake and the nutritional status of patients should be monitored during the course of therapy to ensure adequate intake of nutrients and to prevent nutritional imbalance associated with drug therapy.