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A Medication for Newly Diagnosed Rheumatoid Arthritis in Patient with Lactose Intolerance

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The side effects of rheumatoid arthritis (RA) medication, such as irritation and ulceration of the gastrointestinal mucosa, have been observed and many patients find it difficult to swallow tablets and hard gelatin capsules. This results in a high incidence of noncompliance and ineffective therapy towards treating RA. Fast-dissolving and fast-dispersing drug delivery systems may offer a solution to these problems, and as a result, fast disintegrating tablets are gaining prominence as a new drug-delivery system; one such system is the binding of the active ingredient with lactose. There have been no reports on the rate of lactose intolerance against medication in patients with newly diagnosed RA, because lactose intolerance has not been associated with particular problems with most existing RA therapies. We encounterd a 56-year-old lactose intolerant female patient who had severe diarrhea after receiving drugs to treat her newly diagnosed RA.

Key words: lactose intolerance, rheumatoid arthritis

Rheumatoid arthritis (RA) is a chronic, progressive autoimmune disease that is associated with inflammation, primarily in synovial joints, and affects over 150,000 people in Korea.[1] In recent years, it has become clear that pain and disability caused by disease can be avoided if the disorder is recognized early and treated both promptly and appropriately. Current treatment is strongly dependent on the use of non-steroidal anti-inflammatory drugs (NSAIDs), oral steroids, cyclooxygenase-2 (COX-2) inhibitors, and disease-modifying anti-rheumatic drugs (DMARDs).[2] These drugs are thought to work by suppressing the overactive immune system and are classified as either synthetic or biological. However, the issue of side effects after the administration of these drugs, such as irritation and ulceration of the gastrointestinal (GI) mucosa, has been observed in clinical trials.[3] These gastroenteropathies are generally believed to result from direct contact effects, which can be attributed to the combination of local irritation produced by the free carboxylic group in the molecular structure of the drugs. Thus, the use of conjugation to hide, provisionally, the acidic group of NSAIDs has been proposed as an approach to reduce or to suppress GI irritation due to direct contact effects. In most cases, lactose or glucose is used as a ingredient for conjugation.

Unfortunately, some people are lactose intolerant and are unable to metabolize lactose because they are lacking the required enzyme lactase in the digestive system. It is estimated that 75% of adults worldwide show some deficiency in lactase activity during adulthood. The frequency of decreased lactase activity ranges from as little as 5% in Europe, up to more than 90% in some Asian countries.[4] Approximately 2 to 3% of Koreans are estimated to be lactose intolerant. However, there is no defined protocol for the treatment of those RA patients who are lactose intolerant. In this case study, we report the case of a 56-year-old lactose intolerant female patient who had severe diarrhea after receiving drugs for the treatment of newly diagnosed RA.

CASE REPORT

A 56-year-old woman presented with the chief complaint of right knee pain that had been ongoing for 8 months. Eight months earlier, the patient had visited a different clinic to seek treatment for the same symptoms, was treated with medications, including NSAIDs, but the pain worsened. When visiting our clinic, she com-

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plained of pain and swelling in both proximal interphalangeal joints, metacarpophalangeal joints, with morning stiffness in the right knee for 2-3 hours. We checked her laboratory findings, including radiographs of the knee and hands for confirmation of an inflammatory, autoimmune disease. The laboratory results indicated that the patient had an increased lymphocyte count (51%), a normal level of erythrocyte sedimentation rate/C-reactive protein, and a negative reading for rheumatoid factor, human leukocyte antige-B 27. Upon physical examination of the right knee, the patient had knee swelling, a soft click, and a positive reading on the Mcmurray test. From the radiographs of the knee, a mild narrowing of the medial joint with minimal osteophytes was noted (Fig. 1). We made an initial diagnosis of pathologic plica syndrome with a suspiciously torn medial meniscus that was indicative of an autoimmune disease such as RA; for this reason, a follow-up arthroscopy was performed. From the arthroscopic findings, we determined that the patient had a generalized villous synovitis and a torn medial meniscus (Fig. 2). A synovectomy was performed with a biopsy with partial menisectomy. One week after the operation, the biopsy of the synovium was confirmed by a pathologist as villous hyperplasia with lymphocytic infiltration that favored RA. Based on the patient's history, physical examination, and synovial biopsy, we made the diagnosis of rheumatoid arthritis and treated the patient with medications, including NSAIDs and DMARDs. Three days later, the patient visited our outpatient office complaining of severe diarrhea and general weakness. The patient's lactose intolerance was discovered after her patient history was reevaluated. All of her current medications were stopped, and drugs that did not contain lactose were administered after her diarrhea abated. As a results, her symptoms improved.

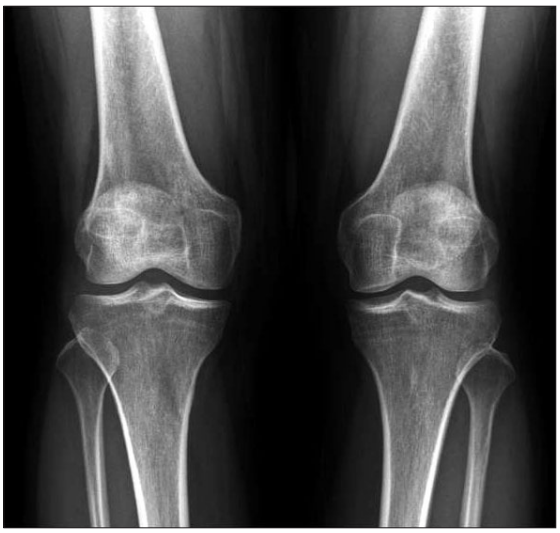

Figure 1. Anteroposterior radiograph shows a mild narrowing of the medial joint with minimal osteophytes.

DISCUSSION

Lactose intolerance is the inability to properly digest lactose, a sugar found in milk and milk products. Lactose intolerance is caused by a deficiency of the enzyme lactase, which is produced by the cells lining the small intestine. Lactase breaks down lactose into 2 simpler forms of sugar called glucose and galactose, which are then absorbed into the bloodstream. The lack of this enzyme may cause a range of abdominal symptoms, including stomach cramps, bloating, and flatulence. In addition, as with other unabsorbed sugars (such as sorbitol, mannitol, and xylitol), the presence of lactose and its fermentation products raises the osmotic pressure of the colon contents, and causes diarrhea. Not all people with lactase deficiency have digestive symptoms, but those who do may have lactose intolerance. Most people with lactose intolerance can tolerate some amount of lactose in their diet.[5]

The treatment of RA is strongly dependent on the lifelong use of NSAIDs, oral steroids, COX-2 inhibitors, and DMARDs. Many patients find it difficult to swallow tablets and hard gelatin capsules

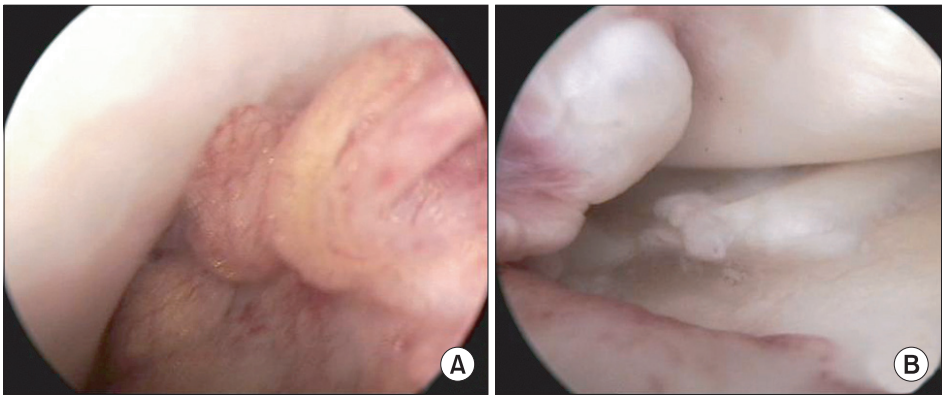

Figure 2. The arthroscopic finding shows generalized villous synovitis (A) and a torn medial meniscus (B).

and, thus, do not comply with the prescription. This results in a high incidence of noncompliance and ineffective therapy.[6] Fast dissolving and fast dispersing drug delivery systems may offer a solution to these problems, and as a result, fast disintegrating tablets (FDT) are gaining prominence as a new drug-delivery system. Other reasons for the need of FDT are the requirements to meet current needs of the industry, like improved solubility, stability, and bioavailability enhancement of poorly absorbed drugs. Various technologies and techniques have been used to manufacture FDT, including freezing, drying, lyophilization, tablet molding, direct compression, spray drying, sublimation, and the addition of superdisintegrants, such as lactose monohydrate, and mannitol.[7,8] In many studies, the effect of lactose excipients on FDT was studied and reported on improving the results of drugs with regard to disintegration time and stability. Therefore, most of the recent medication, especially NSAIDs and DMARDs, contain lactose and mannitol.

There are no reports about medication for newly diagnosed RA of lactose intolerance patients, because lactose intolerance has been thought to not cause particular problems with most existing RA therapies. From the experience of the authors, this case that resulted in stopping the RA medication because of severe diarrhea is thought to be different from general lactose intolerance patients, but additional studies are required. Currently, approximately 30-50% of the domestic Korean population is lactose intolerant, and the number of people suffering from RA is increasing annually. Through the studies of these 2 diseases, we should be able to understand patients in whom these complications occur as the result of medication that contains small amounts of lactose and mannitol. With this knowledge, a proper prevention protocol can be created.

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유당 불내증 환자에서 류마티스 관절염의 약물 치료

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류마티스 관절염의 약물 치료 중 위장관계 부작용은 임상에서 흔히 접하는 문제이다. 대부분의 환자들이 치료를 위해 다양하고 많은 양의 약물을 복용하기를 힘들어 하며, 이러한 문제들로 인해 치료의 순응도가 저하되고 있다. 최근에 이런 문제의 해결 방안으로 약물의 크기를 줄이고, 소화를 빠르게 하기 위해서 약물에 lactose나 glucose 등의 분자를 결합하여 fast-dissolving and fast-dispersing 체계가 고안됐으며, 치료의 순응도가 호전되고 있다. 우리나라 인구 중 유당 불내증의 유병률은 2-3%로 보고되고 있으며, 대부분에서 일상생활에 특별한 문제는 없는 것으로 알려져 있다. 또한, 저자들이 아는 한, 이러한 새로운 체계의 약물과 관련된 설사, 탈수 등의 합병증이 보고된 적은 없었다. 저자들은 유당 불내증이 있었던 56세 여자환자에서 류마티스 관절염으로 진단되어 약물 치료를 하던 중 심한 설사 및 탈수 증세가 발생되어 치료하였던 경험을 보고하고자 한다.

색인단어: 유당 불내증, 류마티스 관절염

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