D-Ribose Supplementation for Rheumatic Diseases

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Abstract
D-ribose is a simple carbohydrate essential for adenosine triphosphate (ATP) synthesis and cellular energy transfer. Reduced high-energy phosphate levels have been documented in fibromyalgia and related conditions, prompting interest in D-ribose supplementation. Following PRISMA guidelines, we systematically searched PubMed, SciELO, and LILACS (1965–May 2024) without language restrictions for studies evaluating supplemental D-ribose in rheumatic diseases. Three studies met inclusion criteria: one prospective open-label trial of 41 patients with fibromyalgia and two case reports (one fibromyalgia, one polyarteritis nodosa with metabolic myopathy). All reported marked clinical improvement in pain, energy, sleep, mental clarity, and overall well-being with D-ribose (typically 5 g two to three times daily); no adverse effects were noted. Although limited by the small number of studies (two of which are case reports), the available data suggest that D-ribose supplementation may be a useful adjunct in fibromyalgia and selected other rheumatic conditions characterized by impaired muscle energy metabolism. Larger, controlled trials are warranted.

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Running head: D-ribose in rheumatic diseases

Introduction

Ribose is a simple carbohydrate that plays a role in high-energy phosphate and nucleic acid synthesis. D-ribose is an energy producing substrate of the adenosine triphosphate (ATP) molecule and presents an essential role in intracellular energy transfer. ATP consists of phosphate, adenosine, and ribose. The ATP stores and transports chemical energy within cells and is essential for synthesis of nucleus acids such as DNA and RNA. In addition, in some diseases such as heart failure, cellular energy deficiency exists in myocardial mitochondria. The reduction in ATP production is directly correlated with the decreased supply of D-ribose in the mitochondria [1,2].

The cellular energy charge may never be fully regained in patients with chronic hypoxic conditions. Supplemental ribose has been shown to enhance the synthesis of adenine nucleotides, rebuilding depressed energy pools in both the heart and skeletal muscle after an ischemic or hypoxic insult [1]. Furthermore, ribose has been shown to improve the energy recovery time in skeletal muscle and to relieve fatigue, soreness, and stiffness after intense exercise. Ribose has also been investigated for its potential medical benefits in cardiovascular disease. Indeed, short- and long-term animal studies found that the use of ribose after myocardial ischemia resulted in enhanced ATP recovery and improved diastolic functional parameters [3]. Studies in patients with fibromyalgia reported a potential abnormality in high-energy phosphate metabolism, as evidenced by significantly lower levels of ATP and ADP in affected muscles compared with controls [4]. Theoretically, the effect of ribose on increasing the muscle energy pool could reduce the metabolic strain in affected muscles and allow patients to assume a more active lifestyle. D-ribose is employed both orally and intravenously in patients for many different pathologic conditions such as chronic fatigue

syndrome, fibromyalgia, and myocardial alterations. Moreover, Ii is often used to improve athletic performance and reduce symptoms of cramping, pain, and stiffness following exercise [2]. Considering the known musculoskeletal symptomatology in this syndrome and the reported benefits of ribose in skeletal muscle metabolism and physiology, we thought to review the studies that evaluated supplemental D- ribose in rheumatic disease, mainly fibromyalgia.

Following PRISMA guidelines, an extensive literature search in PubMed, Scielo, and LILACS was performed, without any language restriction, from 1965 to May 2024. After a review of titles and abstracts, only three articles were selected for this review.

The three articles, in the present systematic analysis, are summarized in table 1 [5-7]. Two studies evaluated fibromyalgia and one a patient with polyarteritis nodosa and metabolic myopathy. Female predominance was noted in the three reports. and ages varied from 37 to 78 years. Two studies were case reports, and one was a prospective study on fibromyalgia, including 41 patients. All articles showed a dramatic improvement in the clinical pictures, including the visual analogic scale for pain, well-being, sleep, and energy levels. No side effects or toxicity were reported. In the case of polyarteritis nodosa and metabolic myopathy [7], the authors treated the patients with D-ribose associated with a diet free of complex carbohydrates, ubiquinone, creatine, carnitine, folic acid, and lipoic acid [7]. It is a limiting factor when analyze that case.

The present study's strengths are 1. the inclusion of all studies on D-ribose in rheumatic conditions; 2. International criteria for rheumatic diseases were applied; 3. PRISMA guidelines for systematic review were used. The limitations are the presence of only three studies, out of which two were case reports. Therefore, future well designed studies using D-ribose in rheumatic conditions are desired to confirm the present data and expand on other rheumatic diseases.

In conclusion, supplementing D-ribose to the therapeutic armament of rheumatic conditions is encouraging, especially in fibromyalgia, myositis and polyarteritis nodosa. There is a need to expand the studies in additional rheumatic entities, applying a well-designed control study on larger populations

Table 1: Studies on D-ribose in rheumatic diseases

Author, year	Study design	Country	Age, gender	N	Disease	D-ribose dosage	Outcome	Side effects
Teitelbaum *et al*., 2006 [5]	Prospective open trial	United States	48 yo, 78% females	41	FM	5g TID	Significant improvement in all five visual analog scale (VAS) categories: energy; sleep; mental clarity; pain intensity; and well-being, as well as an improvement in patient's global assessment. 66% of patients experienced significant improvement D-ribose, with an average increase in energy on the VAS of 45% and improvement in overall the well-being of 30% (*p* _ 0.0001).	None
Gebhart *et al*., 2004 [6]	Case report	United States	37 yo, female	1	FM	5 g twice a day	After 14 days, she improved her sleep and mental alertness and had a a marked decrease in joint pain and normal stools. After 2 months, she was normal.	None
Vishwanath *et al*., 2011 [7]	Case report	United States	78 yo, Female	1	PAN plus metabolic myopathy	She was treated with a diet free of complex carbohydrates and ubiquinone, creatine, carnitine, folic acid, a-lipoic acid and ribose. Dosages are ND.	Dramatic improvement months later.	None

FM: fibromyalgia; ND: not described; PAN: polyarteritis nodosa; TID: three times a day; Yo-years

Declarations

Competing Interests

The author has no conflicts of interest to declare.

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Author Contribution

JF Carvalho has done all partis of this manuscript as Conception, literature search, writing, analysis, submission.

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Availability of Data and Material

All data are available at request.

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