Rheumatoid Arthritis and Osteoporosis: A Case Study

PR Raghavan*  
Nanorx Inc., New York, USA  
*Corresponding author: PR Raghavan, Nanorx Inc., PO Box 131 Chappaqua, New York 10514, USA, Tel: +1-914-671-0224; E-mail: raghavan@nanorxinc.com

Received date: April 21, 2017; Accepted date: April 25, 2017; Published date: May 5, 2017

Copyright: © 2017 Raghavan. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Metadichol® is a Nano emulsion of long-chain alcohols called as Policosanol and is present in foods such as rice, sugar cane, wheat, and peanuts. Metadichol® acts on Nuclear Vitamin D receptors (VDR) that are present in cells throughout the body to stimulate the immune system and inhibit a variety of disease processes, resulting from inflammation to infection [1].

We present a case study of a patient with Rheumatoid arthritis with the high levels of RF antibodies, CRP and ESR levels, and low bone mineral density leading to osteoporosis. The case report shows how Metadichol® by its actions on the VDR has affected key biomarkers and mitigated the disease conditions without any side effects. Also, his bone density improved dramatically.

Metadichol® is safe because it consists of natural components of conventional foods and has no known adverse side effects. Its constituents are present in many foods that we consume every day.

Metadichol® has the potential to serve as a novel, safe solution to help patients with RA and other autoimmune diseases that confront the world today.

Keywords: VDR; Vitamin D; Metadichol®; Innate immunity; Inverse agonist; Protein agonist; Nano emulsion; Long chain lipid alcohols; RA factor; ESR; hs-CRP; TNF-alpha Inhibitors; Osteoporosis; Bone mineral density; BMD

Introduction

Rheumatoid arthritis is a chronic inflammatory disease in which the synovial membrane of the joint becomes inflamed, resulting in a swelling, stiffness, pain, limited motion, joint deformity, and disability. RA is the most common inflammatory arthritis across the world and is an autoimmune disease, in which a person’s immune system attacks his or her healthy tissues [1].

There is no known cure for rheumatoid arthritis, and spontaneous remission in a stable disease is rare. The goal of treatment in this chronic disease today is to alleviate the current symptoms and prevent the future destruction of the joints. These two goals may not always coincide, while pain relievers may achieve the first goal, they do not have any impact on the long-term consequences.

Clinically the Erythrocyte Sedimentation Rate (ESR), C-reactive protein, full blood count, renal function, liver enzymes and other immunological tests are also inflammation indicators in RA patients [2].

Vitamin D has been plays a role in infections like tuberculosis and other no infectious like breast cancer, Vitamin D in conjunction with calcium and phosphorus, maintains healthy bones. High levels of vitamin D decrease the risk of autoimmune diseases, and in reducing the risk of rheumatoid arthritis remains equivocal.

Major immune system-mediated rheumatic conditions such as RA such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) are due to a by low level of vitamin D which has an inverse correlation with the conditions [3-5].

In Osteoporosis more bone is lost than replaced. This loss leads to fragile bones. Osteoporosis patients have lower level of vitamin D in in comparison to those without this condition [6]. Increases Vitamin D level has been shown to prevent osteoporotic fractures. Currently, bone mineral density (BMD) is the biomarker for osteopenia and osteoporosis [7]. With osteoporosis, vitamin D does not to rebuild lost bone density but can decrease rate of bone loss.

Vitamin D, through its active metabolite 1,25(OH)2D3 controls both innate and adaptive immunity but suppressing the adaptive immunity [8,9]. Vitamin D with its immunomodulatory and anti-inflammatory properties is useful in treating RA patients. Vitamin D inhibits Th1 cells and upregulates Th2 cells and thus can block autoimmunity [10,11].

Vitamin D-binding protein (DBP) is a multifunctional plasma protein with many essential functions. It transports vitamin D metabolites, controls bone development, and helps in the binding of fatty acids, sequestration of actin, and a range of less-defined roles in modulating immune and inflammatory responses [12]. It transports vitamin D to liver, kidneys, bone, and other target tissues, and stores and increases the half-life of the circulating vitamin D metabolites. As such, Vitamin D metabolites are firmly and positively correlated with DBP levels in serum [13].

DBP can also be converted to a macrophage activating factor (DBP-MAF) by the deglycosylation of DBP that can modulate osteoclast differentiation and bone resorption by directly activating osteoclast. DBP-MAF increase because of inflammatory conditions that leads to more osteoclast activity [14-17].
TNF is another important cytokine that also has a role in host response to inflammatory conditions. It role in many in the pathogenesis of inflammatory diseases such as rheumatoid arthritis (RA), psoriasis, psoriatic arthritis, and inflammatory bowel disease is well established [18].

Inhibition of TNF-α is an approach to treating rheumatoid arthritis [18]. Infliximab®, Enbrel®, and Humira® are TNF-alpha inhibitors that are FDA-approved for treatment of RA. TNF inhibition dramatically reduces markers of inflammation, but it also slows or halts the structural damage which appears to be as potent in early disease as they are in late disease. These drugs used for the treatment of patients with chronic inflammatory disorders. There is however a downside with an increased risk of Tuberculosis [19-21]. There is a need for a safe and effective drug in treatment of such diseases.

Patient Case Presentation

We have a case report on a 60 years old male patient with rheumatoid arthritis for the last 18 years. Over the years, his condition has led to low bone mineral density, resulting in osteoporosis. His regular treatment was monthly injections of cortisones and daily use of Tylenol. The patient was not on any TNF-alpha inhibitors. Before this case study, his CRP level over 2+ years ago was all normal (below 2), but it has started creeping up within the last two years. Two weeks before treatment with Metadichol, his CRP level has climbed from 27 to 83 (at baseline). After using Metadichol, his CRP has dropped back to 2 within the first 16 weeks and is remained under control over the next 62 weeks. His ESR has also shown significant improvement from 105 at baseline to 80 at week 36 and 40 at week 78. His RA Factor dropped from 698 at baseline to 190 at week 24, and 58 at week 78. The treatment results with Metadichol and the improvement on his biomarkers are indicated in Figures 1-6.

Discussion

Metadichol rapidly acted to reduce ESR and CRP levels. The RA factor showed a significant reduction.

Metadichol, as we have shown, is an inverse agonist of VDR, and all inverse agonists block constitutive response. We have shown Metadichol exhibits dual properties such as increasing insulin secretion [22] and reducing insulin in patients with type 2 diabetes [1]. It is likely a Protean agonist, which can act both as positive and negative agonists on the same receptor, depending on the degree of constitutive activity that is present. If there is no constitutive activity, the agonist would be an active agonist. When the constitutive activity is present, the Protean agonist would be an inverse agonist [23].

Elevated levels of CRP and ESR are associated with disease severity in RA [24,25]. Our results show that Metadichol has successfully lowered both CRP and ESR for the RA patient. His RA factor has also decreased rapidly. The more striking finding was the improvement in bone density as seen in Figures 4-6.

Osteoporosis is a condition in which the bone mineral density (BMD) is 2.5 standard deviations below that of a young healthy, gender-matched group (T less than -2.5). Osteopenia is defined as bone mineral density that is 1 to 2.5 standard deviations below that of a healthy sex-matched population (T-score between -1 and 2.5). BMD less than -2.5 and with bone fracture indicates severe osteoporosis.

According to International Society for Clinical Densitometry, the WHO criteria for osteoporosis applies to postmenopausal and perimenopausal females and men over 60 years [24]. For all other patients, the Z-score should be used with a cut off the standard of more than -2.0 [26].
Many useful drugs act via modulation of multiple proteins rather than single targets. Some protein kinase inhibitors like Student and Gleevec, act on multiple signaling kinases [27].

Yıldırım et al. suggest that many keys open a lock rather than one key to open many locks [28]. Mitigating disease states may require a drug to act via multiple pathways to be potent, because affecting multiple biological networks is more important than single targets. Such an approach has been highlighted and advocated by Andrew Hopkins [29].

Effective drugs act via modulation of multiple proteins rather than single targets. Metadichol does just that.

It mode of action is by optimizing multiple activities, and balancing drug-like properties and eliminating undesirable off target effects. The inverse/protein property exhibited by Metadichol leads to many pathways it modulates by targeting, VDR, PPAR gamma as well as inhibition of cytokines like TNF-alpha, MCP-1, PAI-1 and the endogenous increase of Vitamin C levels which we have shown in our Rat studies [1]. Given the range and breadth of actions of Metadichol the results suggest that it mimics the effects of 1,25-dihydroxy Vitamin D3 but without the toxic effect secondary to Calcemia that has its use as a pharmaceutical agent [30]. Metadichol is the first example of a smart molecule that can simultaneously modulate multiple targets which can with Metadichol can lead potentially to a successful treatment of many of these challenging diseases [31-35].

More clinical studies with Metadichol studies are planned, and hopefully, it will be lead to overcoming RA and in improving bone density which is of great importance in aging populations. Metadichol can be useful an anti-inflammatory molecule and has been shown to have toxicity at doses of up to 5000 mg/kg [36]. Metadichol can be useful in treating chronic diseases like RA.

Using the criteria mentioned above, at baseline, the patient has osteoporosis in his right femur with an increased risk of fragility fractures and in his left femur with an increased risk of fragility fractures by a factor of six which is five times more than normal. The bone mineral density of his lumbar spine and right forearm was in the normal range.

After treatment with Metadichol for 52 weeks, the bone mineral density of femoral and right forearm was in the normal range. BMD of the lumbar spine normalized at 52 weeks. There is a definite improvement when compared to his baseline BMD of femoral.

Metadichol treatment led to the lower levels of the important inflammation biomarkers and alleviated his pain and increased his mobility. Today's approach in drug research is a lock (drug target) and a key (drug) Given the many side effects of drugs, and to overcome it the search for high selective ligands has been the approach of the drug discovery community, and that has proven to be cost and time consuming without any tangible benefits.

References


