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Effect of Vegan Diet On Patients With Rheumatoid Arthritis: A Mini Review.

Usha Adiga^{1*}, and Sriprajna Mayur².

¹Professor, Dept of Biochemistry, KS Hegde Medical Academy, Nitte –DU, Mangalore, Karnataka, India.

²Research Scholar, Central Research Scholar, KS Hegde Medical Academy, Nitte –DU, Mangalore, Karnataka, India.

ABSTRACT

Rheumatoid arthritis (RA) is a systemic, debilitating, chronic inflammatory autoimmune disorder. There are interventional studies in which vegan, mediterranean and elementary diet were administered in different patient populations and have proven to be beneficial. There are only few studies available to the best of our knowledge which have reviewed effect of diet on RA. Objective of this mini review is to discuss the influence of various diets on clinical outcome of RA and to propose a possible beneficial role of a combination diet on improving RA which can be monitored through biomarkers.

Keywords: nutritional formula. rheumatoid arthritis, biomarkers

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Corresponding author

BACKGROUND

Rheumatoid arthritis (RA) is a systemic, debilitating, chronic inflammatory autoimmune disorder affecting approximately 1% of the world population (1). The disease severely impacts quality of life with increased morbidity and reduced life expectancy. With the rapidly expanding population with RA, the disease has put a lot of economic burden on the society.

With undefined pathogenesis, different studies report a blend of environmental, immunological and genetic factors responsible for full expression of the disease. These factors, however, contribute approximately 50% to the risk of development of RA while the rest may be contributed by host–environment interactions(2).

Patients with RA generally complain of gastrointestinal tract problems particularly dyspepsia (bloating, postprandial fullness, nausea, early satiety, epigastric pain, and burning and belching), mucosal ulceration, and altered bowel habits (constipation/diarrhea) (3). An altered intestinal microbiota has thus been implicated in the etiopathogenesis of RA (4-6). Recently, Littman laboratory identified *Prevotella copri* significantly prevalent in RA patients than healthy controls providing the support that the “gut-joint axis” hypothesis is relevant for human rheumatic diseases and may lead to pathogenesis of RA (7).

Dietary Interventions in RA

With the increasing evidence of altered microbiota in the gut of RA patients being responsible for pathogenesis as well as disease progression, it would be desirable to advocate a supplemental “diet therapy” to RA patients(5,7). Various dietary plans for RA have been reported since long (8) and are being repeatedly projected (9-13), such as vegan (14-17) or Mediterranean diets (18). This has been repeatedly reported that vegan diet is clinically beneficial for disease remission in RA patients (44–46). Studies conclude that the improvements in disease activity might have been a result of reduction in immune-reactivity to certain food antigens in the gastrointestinal tract that were eliminated by changing the diet (14-16).

Mediterranean diet is rich in oleic acid, omega-3 fatty acids, unrefined carbohydrates, and phytochemicals. A study conducted by Sköldstam et al. concluded that on administration of Mediterranean diet to RA patients, inflammation was reduced, vitality and physical functions were improved (18).

Rosillo et al. have shown that administration of extra virgin olive oil in CIA mice (type II collagen-induced arthritis) reduced the serum levels of cartilage oligomeric matrix protein (COMP) and metalloproteinase-3 (MMP-3) that are the predictive markers of cartilage and joint damage in RA due to antioxidant property. The expression of pro-inflammatory cytokines including IL-1 β , TNF- α , and IL-17, involved in progression of the disease, was also reduced. The study concluded that mice fed with olive oil had reduced cartilage destruction, joint edema, and arthritis development, and thus, olive oil may be beneficial in preventing RA (19).

Elemental diet provides food in simplest form consisting of glucose, vitamins, trace elements, and essential amino acids, is hypoallergenic, contains all nutrients for daily requirements, and is thought to be less immunogenic. In the clinical trial conducted by Podas et al. (20), RA patients were given an elemental diet for 2 weeks. A large proportion of patients (72%) taking this elemental diet had more than 20% improvement in pain, early morning stiffness, and the Ritchie articular index (RAI). Similarly, Kavanagh et al. and Holst-Jensen et al. reported effects of different elemental diets with improvement in clinical and symptomatic parameters helping patients with food-aggravated disease conditions(21,22). Patients treated with elemental diet showed reduced symptoms of RA but relapsed on discontinuation (21).

Biomarkers in RA

Various biomarkers have been developed which can predict the severity of the disease progression, monitorization of disease evolution and responsiveness to therapy. As per “treat to target” recommendations, 3 composite scores for the monitorization of the disease evolution used are: disease activity score (DAS 28), simple disease activity index (SDAI) and clinical disease activity index (CDAI). For a better monitorization of the disease activity, a test that includes several biomarkers under the name “multi-biomarkers disease activity test (MBDA)”.

The introduction of biological therapies in the management of RA represented a major step forward for a better control of the disease. High costs and patient exposure to severe adverse reactions determined the need to identify biomarkers that can distinguish pretreatment responders vs. nonresponder patients. Over time, several potential biomarkers were tested and identified with this role, but none were adopted in practice.

In a study that included 279 patients with early forms of RA, followed for five years by clinical examination, serological and imaging tests, the presence of anti-CCP at diagnosis was associated with a more important radiological progression and severe forms of disease (23). Serum markers like anti-MCV, cartilage oligomeric matrix protein (COMP) and serum calprotectin were the markers tested in order to know the responsiveness to therapy (24-29). High levels of calprotectin can appear in RA and other various inflammatory conditions [25]. Survivin, a tumoral biomarker, which belongs to the family of inhibitors of apoptosis, has been reported in patients with RA [26].

Aim of this review was to propose on administration of vegan diet which is a combination of nutrients of Mediterranean and elemental diet which may be proved beneficial for rheumatoid arthritis in relieving symptoms by reducing inflammation and as well as by increasing the responsiveness to therapy. The beneficial effect of diet may be assessed clinically as well as by monitoring serum biomarkers.

There are interventional studies in which vegan, Mediterranean and elementary diet in different patient populations and have proven to be beneficial. But a nutritional formula, which includes all the components of above mentioned three types of diet can be formulated, efficacy of which can be tested clinically, as well by assessing serum biomarkers. There are only few studies available to the best of our knowledge which have similar study design.

Future Perspectives

A research study can be carried out to test the efficacy of the vegan diet in improving symptoms of RA patients. In addition, the serum biomarkers which predict prognosis, monitor disease severity and responsiveness to therapy among RA patients who are on vegan diet and those without supplementation can be compared.

Expected outcome of such research endeavour

- If the study results prove the efficacy of the vegan nutritional formula, its regular supplementation to RA patients may be recommendable.
- This may help in improving the symptoms, slow down the disease progression, may enhance patients responsiveness to pharmacological treatment.
- Such diet may be a cost effective adjunct therapy, if it reduces the dosage of drugs required.

REFERENCES

- [1] Gibofsky A. Overview of epidemiology, pathophysiology, and diagnosis of rheumatoid arthritis. *Am J Manag Care* 2012; 18(13):S295–302.
- [2] Edwards CJ. Commensal gut bacteria and the etiopathogenesis of rheumatoid arthritis. *J Rheumatol* 2008;35(8):1477–9
- [3] Wolfe F, Kong SX, Watson DJ. Gastrointestinal symptoms and health related quality of life in patients with arthritis. *J Rheumatol* 2000;27(6):1373–8.
- [4] Gul'neva M, Noskov S. Colonic microbial biocenosis in rheumatoid arthritis. *Klin Med* 2010;89(4):45–8.
- [5] Vaahrovuo J, Munukka E, Korkeamäki M, Luukkainen R, Toivanen P. Fecal microbiota in early rheumatoid arthritis. *J Rheumatol* (2008) 35(8):1500–5.
- [6] Toivanen P. Normal intestinal microbiota in the aetiopathogenesis of rheumatoid arthritis. *Ann Rheum Dis* 2003;62(9):807–11.
- [7] Scher JU, Sczesnak A, Longman RS, Segata N, Ubeda C, Bielski C, et al. Expansion of intestinal *Prevotella copri* correlates with enhanced susceptibility to arthritis. *Elife* 2013;2:e01202.10.7554/eLife.01202

- [8] Panush RS, Carter RL, Katz P, Kowsari B, Longley S, Finnie S. Diet therapy for rheumatoid arthritis. *Arthritis Rheum* 1983; 26(4):462–71.
- [9] Vitetta L, Coulson S, Schloss J, Beck SL, Allen R, Sali A. Dietary recommendations for patients with rheumatoid arthritis: a review. *Nutr Diet Suppl* 2012; 4(4):1–15.
- [10] James MJ, Cleland LG. Dietary n-3 fatty acids and therapy for rheumatoid arthritis. *Semin Arthritis Rheum* 1997;27(2):85–97.
- [11] Darlington L, Ramsey N, Mansfield J. Placebo-controlled, blind study of dietary manipulation therapy in rheumatoid arthritis. *Lancet* 1986;327(8475):236–8.
- [12] Kremer J, Michalek A, Lininger L, Huyck C, Bigauoette J, Timchalk M, et al. Effects of manipulation of dietary fatty acids on clinical manifestations of rheumatoid arthritis. *Lancet* 1985; 325(8422):184–7.
- [13] Kremer JM, Lawrence DA, Jubiz W, Digiacomio R, Rynes R, Bartholomew LE, et al. Dietary fish oil and olive oil supplementation in patients with rheumatoid arthritis clinical and immunologic effects. *Arthritis Rheum* (1990) 33(6):810–20.
- [14] Kjeldsen-Kragh J, Haugen M, Borchgrevink C, Førre Ø. Vegetarian diet for patients with rheumatoid arthritis-status: two years after introduction of the diet. *Clin Rheumatol* 1994;13(3):475–82
- [15] Hafström I, Ringertz B, Spångberg A, Von Zweigbergk L, Brannemark S, Nylander I, et al. A vegan diet free of gluten improves the signs and symptoms of rheumatoid arthritis: the effects on arthritis correlate with a reduction in antibodies to food antigens. *Rheumatology* 2001; 40(10):1175–9.
- [16] McDougall J, Bruce B, Spiller G, Westerdahl J, McDougall M. Effects of a very low-fat, vegan diet in subjects with rheumatoid arthritis. *J Altern Complement Med* 2002;8(1):71–75
- [17] Haugen M, Kjeldsen-Kragh J, Skakkebaek N, Landaas S, Sjaastad Ø, Movinkel P, et al. The influence of fast and vegetarian diet on parameters of nutritional status in patients with rheumatoid arthritis. *Clin Rheumatol* 1993;12(1):62–9.
- [18] Sköldstam L, Hagfors L, Johansson G. An experimental study of a Mediterranean diet intervention for patients with rheumatoid arthritis. *Ann Rheum Dis* 2003; 62(3):208–14.
- [19] Rosillo MA, Sánchez-Hidalgo M, Sánchez-Fidalgo S, Aparicio-Soto M, Villegas I, Alarcón-de-la-Lastra C. Dietary extra-virgin olive oil prevents inflammatory response and cartilage matrix degradation in murine collagen-induced arthritis. *Eur J Nutr* 2016;55(1):315–25.
- [20] Podas T, Nightingale JM, Oldham R, Roy S, Sheehan NJ, Mayberry JF. Is rheumatoid arthritis a disease that starts in the intestine? A pilot study comparing an elemental diet with oral prednisolone. *Postgrad Med J* 2007; 83(976):128–31.
- [21] Kavanagh R, Workman E, Nash P, Smith M, Hazleman B, Hunter J. The effects of elemental diet and subsequent food reintroduction on rheumatoid arthritis. *Rheumatology* 1995;34(3):270–3.
- [22] Holst-Jensen SE, Pfeiffer-Jensen M, Monsrud M, Tarp U, Buus A, Hesselø I, et al. Treatment of rheumatoid arthritis with a peptide diet: a randomized, controlled trial. *Scand J Rheumatol* 1998;27(5):329–36.
- [23] Qianwen L, Yufeng Y, Xin L, Guangliang S, Xuan Z. The Status of Rheumatoid Factor and Anti-Cyclic Citrullinated Peptide Antibody Are Not Associated with the Effect of Anti-TNF α Agent Treatment in Patients with Rheumatoid Arthritis: A Meta-Analysis. *PLOS ONE* 2014;9:1–10.
- [24] DeJaco C, et al. Antibodies against mutated citrullinated vimentin fail to predict anti-TNF α treatment response in rheumatoid arthritis. *Scand J Rheumatol* 2009;38(1):66–67.
- [25] Fabris M, De Vita S, Blasone N, Visentini D, Pezzarini E, Pontarini E, Fabro C, Quartuccio L, Mazzolini S, Curcio F, Tonutti E. Serum levels of anti-CCP antibodies, anti-MCV antibodies and RF IgA in the follow-up of patients with rheumatoid arthritis treated with rituximab. *Auto Immun Highlights* 2010;1(2):87–94.
- [26] Marotta A, Maksymowich WP. SAT0070 Levels of 14-3-3 ϵ Predict Good Eular Response to Anti-TNF Treatment in Patients with Rheumatoid Arthritis. *Ann Rheum Dis* 2014;73:615–616.
- [27] Sagawa A, Kaneda M, Gui Y, Marotta A, Arai J. Evaluation of Serum 14-3-3 ϵ Levels in A Japanese RA Cohort Treated with Tocilizumab. *Ann Rheum Dis* 2014;73
- [28] Morozzi G, Fabbroni M, Bellisai F, Cucini S, Simpatico A, Galeazzi M. Low serum level of COMP, a cartilage turnover marker, predicts rapid and high ACR70 response to adalimumab therapy in rheumatoid arthritis. *Clin Rheumatol* 2007;26(8):1335–1338.
- [29] Choi IY, Gerlag DM, Herenius MJ, Thurlings RM, Wijbrandts CA, Foell D, Vogl T, Roth J, Tak PP, Holzinger D. MRP8/14 serum levels as a strong predictor of response to biological treatments in patients with rheumatoid arthritis. *Ann Rheum Dis* 2015;74(3):499–505.



- [30] Isgren A, Forslind K, Erlandsson M, Axelsson C, Andersson S, Lund A, Bokarewa M. High survivin levels predict poor clinical response to infliximab treatment in patients with rheumatoid arthritis. *Semin Arthritis Rheum* 2012;41(5):652–657.