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Review Article

Understanding Dynamics: Probing into Gut Health and Dietary Interventions on Biomarkers of Inflammation in Rheumatoid Arthritis

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ABSTRACT

It Rheumatoid arthritis (RA) is a debilitating and disabling autoimmune disorder characterized by joint pain, stiffness and lost muscle function. About 1% of population accounts for individuals suffering from this disease and 30% of RA patients find it difficult to perform daily task in a span of next 10 years of the onset of the condition. Moreover, it is observed that women are more affected than men between the ages of 40-70 years; children are also affected at any age. It causes painful inflammation and subsequent cartilage and bone destruction owing to pro inflammatory triggers like IL-6, cytokines, TNF- with no clear signs in the starting. Current drug treatment for treating rheumatoid arthritis is expensive and deleterious on overall health on long-term use. Gut abnormalities can be an underlying cause of disease activity in RA. RA in a pre-disposed condition starts in the gut and may run in the families.

Early diagnosis and remission period can prevent damage to the joints and restore lost muscle function in RA. There are some anti-inflammatory foods providing relief from the unpredictability of damages occurring through biomarkers of inflammation that increases disease activity in RA patients. There is a need of extensive studies addressing the interaction between nutrients and pro-inflammatory response in RA pathogenesis.

Keywords: RA; TNF-; IL-6; Cytokines; Ant-inflammatory foods

INTRODUCTION

Disease activity in RA, an auto-immune disorder wherein immune system wrongly attacks your body which is basically responsible for protection against foreign antigens such as viruses and bacteria, is marked by two inflammatory biomarkers that is, ESR (Erythrocyte Sedimentation Rate) and CRP (C-reactive protein). The most compelling reason for auto-immune condition resides in the intestinal lining of an individual suffering from the disease, even before the symptoms augments.

Rheumatoid Arthritis (RA) is an inflammatory condition denoted by 'rheumatoid cachexia' a term for generalized muscle loss in RA patients. Not all genetically predisposed to RA develop the disease. Research on possible key reason for occurrence of RA is a complex interaction between genetic alteration, environment condition and potential triggers like specific nutrients. Furthermore, deleterious effect of an impaired immune-regulatory condition along with different pro-inflammatory triggers has annoyed this problem [1]. This condition has remarkable impact on physical function, strength and quality of life in RA patients [2].

To date, conventional triggers for the onset of the disease known are microbial agents, chronic stress and cigarette smoking suggests a possible reason. But, there are meager reports on nutritional factors as latent cause of onset, perpetuation and long-term effect of the disease via epigenetic mechanism [3].

Anti-inflammatory diets can improve the deleterious effects of pro-inflammatory triggers. This review highlights the impact of diet on disease activity in RA condition through dietary intervention and protein supplementation.

Specific compounds in food provides primed defense boosting up against inflammatory response under certain threshold limit of nutrients in the modified diet by decreasing disease activity.

THE AUTOIMMUNE TRIAD-WHAT DOES IT DO?

The autoimmune response in RA is multi factorial that involves increased intestinal permeability, genetic pre-disposition and antigen reaction to exposure [4].

BIOMARKERS OF INFLAMMATION IN RA-

IL-6: A cytokine produced by cells of immune system, vascular endothelial cells, adipocytes and skeletal muscles.

TNF-: A cytokine produced by lymphoid cells, mast cells, vascular endothelial cells, cardiac myocytes, adipocytes, fibroblasts and

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neural tissue.

CRP: Acute phase protein produced by liver

Visceral adiposity and an increase in fat diet increases levels of pro-inflammatory cytokines as with age body fat shifts to abdominal/visceral fat stores than subcutaneous fat. Increased fat diet is directly involved in higher levels of IL-6, TNF-α whereas Mediterranean diet decreases their levels [5].

The grade of disordered metabolism in adults with RA is correlated with the amount of IL-1 and TNF induced by peripheral blood mononuclear cells [6]. Studies shows that elevated level of these pro-inflammatory triggers are indicators of disability in RA in older patients.

INTER-RELATIONSHIP BETWEEN INFLAMMATION AND ITS BIOMARKERS-

Every second our life is under attack of millions of bacteria, viruses and spores that tries to invade the body and engulfs its resources for itself. The immune system is at rescue to fight like an army of cells and guard against foreign antigens. But, in RA this system of protection gets disrupted wherein body's own immune cells mistakenly invades its own cells.

During a condition of infection, foreign antigens via wound cease the opportunity to enter inside the body and spreads by doubling their number using body's nutrients reservoir every 20 minutes. To this changed environment inside the immune system firstly, macrophages/guard cells engulfs them and destroy with the help of enzyme by trapping inside a membrane. The primary function of macrophages is to kill enemies for example foreign antigen and its secondary function is activation of cells, signaling and onset of inflammation.

Inflammation via a messenger protein communicate with neutrophils in the blood vessels, that kills healthy cells along with foreign cells and commit suicide in five days to decrease harm to other cell. Dendrite cells in brain also get activated and signals T-cells and B-cells consequently to target the antigens from outside the body working in a complex system.

THE GUT PHYSIOLOGY IN RA: A CASCADE OF INTERACTIONS

In living organisms, the intestine forms the mucosal interface with environment separating blood stream and the matter inside the intestine. The intestine facilitates nutrients inside the body by excreting toxins, bacteria and other wastes outside the body and maintaining optimal gut micro biome. But, the epithelial cells are not cemented tightly and can lead to increased permeability in intestine, termed as leaky gut. These impaired tight junctions possibly result in incomplete absorption of digested protein and antigen that can spur immune system via bloodstream.

Many research findings have showed that the abundance of Prevotella copri is redoubled in some early diagnosed RA patients. Moreover, some genobiotic experiments indicated the occurrence of dysbiosis in RA patients lead to occurrence of Th-17 cell dependent inflammatory disease in enteral microbiota-humanized SKG mice. Recent studies have revealed that over 100 genetic susceptible sites are involved in pathogenesis of RA. It has also been observed that ACPA (anti-citrullinated protein antibody), an immunoglobulin is detectable before the outset of RA suggesting that RA originates at mucosal sites, the mouth and the gut. A major pathogenic bacterium of periodontal disease known as Porphyromonous gingivalis, expresses a peptidylarginine deiminase that can be related to ACPA in arthritis.

An altered intestinal microbiota has been observed evidently with recent-onset of RA in many countries, as segmented filamentous bacteria (SFB) over stimulates TH 17 cells in the gut and triggers arthritis in mice [7].

MICROBIOME AND DIET - A DOMINO EFFECT IN RA-

A modified microbiome acts as adjunct therapeutic approach in subliming inflammation in both animal and human models. The gut science in RA is an emerging defense response as they play key role in optimization of immune system. Since birth it takes about few years to develop healthy bacteria that are around in millions from about 5000 species. The microbiome thus developed is determined by what we eat. Gut bacteria stimulate immune cells in the gut to send signal in brain cells to recover from injury.

Consumption of cherries decreases CRP and nitric oxide but more extensive research needed for treatment of disease. Increased omega 6 and omega 3 Fatty acid ratio acts as pro-inflammatory and gamma linolenic acid are anti-inflammatory in nature. Taking supplements of calcium and vitamin D decreases the risk factor of osteoporosis and helps in lowering in pro-inflammatory cytokines.

The active metabolite of vitamin D prohibits the production of several tumour necrosis factor and interleukin and thereby decreases the impression of pro-inflammatory surface molecules. For the short term period vitamin D supplementation has been observed to lessen disease activity in RA patients. The anti-inflammatory effect of flavonoids is exerted through varied mechanisms, largely shared by most flavonoid compounds, and these mostly embody the direct or indirect inhibition of pro-inflammatory cytokines through the immunomodulation of chief inflammatory communication cascades, the diminished enlisting of pro-inflammatory cell subsets, their magnified inhibitor properties, and their beneficial impact on immunoregulatory functions. Recent evidence has steered that flavonoids is potential modifiers of adaptive and innate immunity.

CONCLUSION

Research efforts concerning the use of vitamin D supplements in treatment of inflammation are still considered under-exploited. One of a kind of research characterized the vitamin D insensitivity in both peripheral blood and inflamed joints of patients having inflammatory disease. On contrary, the most plausible explanation for less effect of vitamin D in treating inflammation is due to vitamin D insensitivity in RA.

The pathogenesis of RA involves systemic inflammation that leads to further development of disease activity. Amongst various changes at biological level during initiation of inflammation, remains a challenge to researchers because of its unprecedented onset, progression that constantly interferes with healthy tissues of the body.

New dietary interventions approaches of many kinds plays a significant role in analysis and identification of possible biomarkers of RA and considering diet and protein supplement as a crucial part of RA treatment to decrease disease activity and its progression.

RECOMMENDATION

Recent studies indicate that maintaining an optimal level of vitamin D may help to avert the onset of RA. Since dietary intake of vitamin D of many people is below their suggested adequate intake values, strategies to successfully to recondition the vitamin D insensitivity of immune cells viz. specific T-cells requires much higher doses of vitamin D.

EGCG (epigallocatechin gallate), a phytochemical compound found in green tea, endows anti-inflammatory properties. EGCG targets TAK1, a protein that facilitates pro-inflammatory cytokines transmit their inflammation causing signals in FLSRA.

A reduction in consumption of trans fat, generally found in processed food have been recognized to markedly reduce levels of IL-6 and CRP, biomarkers of inflammation.

Arachidonic acid, a precursor to pro-inflammatory triggers such as leukotrienes and prostaglandins prominent in Western diet. These conditions can be reversed by incorporation of fish oil supplements.

Association between inflammatory diets and RA has driven researchers to attempt to rationally harness healing properties of anti-inflammatory foods. To this end, dietary interventions and protein supplements are gaining increased acceptance for a myriad of potentially beneficial effects, including anti-inflammatory and cardio protective effects and decreased bone erosion. There are still contraindications regarding Fe supplement for anemia condition in RA only up to RDA.

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