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The potential effect of probiotics on rheumatoid arthritis: a systematic review and meta-analysis

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Review question(s)
In this study we aim to systematically review and meta-analyze the effect of probiotics supplementation on disease activity and symptoms in patients with rheumatoid arthritis.

Searches
Nine electronic databases including PubMed, Scopus, Google Scholar, ISI Web of science, WHO Global health library, POPLINE, VHL, NYAM (New york academy of medicine) and SIGLE (System for information on grey literature in Europe) will be used to conduct electronic search for relevant studies using the research term.

There is no restriction regarding to language, publication period or population

Types of study to be included
Except for review articles and book chapters, all types of articles reporting relationship between the disease and intervention are included .

Condition or domain being studied
Rheumatoid arthritis (RA) is an inflammatory systemic autoimmune disease that primarily affects the joints; its etiology has not been fully described yet. Between 0.5% and 1% of adults in developed countries have rheumatoid arthritis, with 5 to 50 new reported cases per 100,000 people each year [1]. Onset is most frequent during middle age and women are affected 2.5 times as frequently as men [2]. RA hallmark feature is chronic symmetric polyarthritis; involvement of extra-articular organ is also common. This condition progresses gradually and leads to major complications if not treated properly. There is no long-term treatment that provides consistent relief without adverse effects and so there is a real need for safe and effective alternatives. Probiotics have been defined by the World Health Organization and the Food And Agriculture Organization as "live microorganisms which, when administered in adequate amounts, confer a health benefit on the host" [3], they have been documented to have beneficial effects on multiple systems in humans and in animals[4], some evidence suggested that probiotics strengthen the immune system, affect both the innate and adaptive immunity [5]. Some strains are also thought to have a role in regulating cytokines function and modulating inflammatory and hypersensitivity responses [6]. With numerous studies suggesting positive effects of probiotics in regulating immune response, we aim to systematically review and meta-analyze all studies published in the literature that are related to the effects of probiotics on activity and symptoms of rheumatoid arthritis and provide hard evidence regarding its benefits and harms for patients with this particular condition.

References:

[1] Scott DL, Wolfe F, Huizinga TW (Sep 25, 2010). "Rheumatoid arthritis". Lancet 376 (9746): 1094–108.

[2] National Institute of Arthritis and Musculoskeletal and Skin Diseases. August 2014. Retrieved 2 July 2015.

[3] Anonymous (2002) Guidelines for the evaluation of probiotics in food, Food and Agriculture Organization of the

United Nations and World Health Organization Expert Consultation Report.
http://www.who.int/foodsafety/publications/fs_management/ probiotics2/en. 11–1. [Cited 5 January 2012].

[4] Magdalena Araya, Catherine Stanton, Lorenzo Morelli, Gregor Reid, Maya Pineiro, et al., 2006, "Probiotics in food: health and nutritional properties and guidelines for evaluation," Combined Report of a Joint FAO/WHO Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics in Food Including Powder Milk with Live Lactic Acid Bacteria, Cordoba, Arentina, 1–4 October 2001, and Report of a Joint FAO/WHO Working Group on Drafting Guidelines for the Evaluation of Probiotics in Food,London, Ontario, Canada, 30 April–1 May 2002 [FAO Food and Nutrition paper 85], pp. 1–50, Rome, Italy:World Health Organization (WHO), Food and Agricultural Organization (FAO) [of the United Nations],

[5] Delcenserie V, Martel D, Lamoureux M, Amiot J, Boutin Y, Roy D (2008) Immunomodulatory effects of probiotics in the intestinal tract. Curr Issues Mol Biol 10, 37–54.

[6] Reid G, Jass J, Sebulsky MT, McCormick JK; Jass; Sebulsky; McCormick (October 2003). "Potential uses of probiotics in clinical practice". Clin. Microbiol. Rev. 16 (4): 658–72.

Participants/ population

Our Inclusion Criteria are as follows: Any paper published until November 2015 that have the following criteria:

1). Current clinical trials,case reports,case series and observational studies discussing probiotics on rheumatoid arthritis.

2) Reporting data on Human

3) No restriction on race, age, sex , place, ethnicity, or language

4) No restriction on publication date

Exclusion criteria

1) Human subjects with multiple autoimmune diseases

2) In-vitro or non-human studies

3) Reviews, letter, editorial, thesis, Or news

4) Data cannot be extracted

5) Overlapped data set

6) Only abstract articles or book chapter

Intervention(s), exposure(s)

Intervention: probiotics supplementation

Comparator(s)/ control

When there are control groups such as another drug or placebo, the comparison will be considered.

Context

Inclusion criteria:

1). Current clinical trials,case reports,case series and observational studies discussing probiotics on rheumatoid arthritis.

2) Reporting data on Human

3) No restriction on race, age, sex , place, ethnicity, or language

4) No restriction on publication date

Exclusion criteria:

1) Human subjects with multiple autoimmune diseases

2) In-vitro or non-human studies

3) Reviews, letter, editorial, thesis, Or news

4) Data cannot be extracted

5) Overlapped data set

6) Only abstract articles or book chapter

Outcome(s)

Primary outcomes

Assessing the effect of probiotics supplementation on:

1. Severity of symptoms and inflammation in previously affected joints.

2. Progress of RA and number of affected joints.

3. Concentration of pro-inflammatory cytokines.

Secondary outcomes

To find a relationship between probiotics and pathogenesis of Rheumatoid Arthritis.

Data extraction, (selection and coding)

Three independent reviewers will extract the data from the selected papers to avoid bias using a standardized form after training and pilot step. Discrepancies will be solved through discussion and consensus among the researchers. When there is missing data and data error the corresponding author or the first author will be contacted via email for clarification. If no response the data will be considered missing. Trials published by the same research group will be checked for duplication

Risk of bias (quality) assessment

Three reviewers will independently evaluate the methodological quality of the included papers across several metrics including study design, full description of characteristic of subjects, data collection (prospective or retrospective), inclusion criteria, exclusion criteria, method quality assessment (such as detailed description and same method for case and control groups), and blinded interpretation of variables. Publication bias will be carried out by Egger's regression test and the trim and fill method of Duvall and Tweedie. We will also conduct the sensitivity, meta-regression and subgroup analyses to study the effect of each co-variate on the pooled results if applicable

Strategy for data synthesis

In papers that discuss the same comparison, Meta-analysis will be done for particular variables using RevMan software version 5.3 for window.

Analysis of subgroups or subsets

Doing subgroup analysis will be decided depending on several co-variates extracted.

Contact details for further information

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Organisational affiliation of the review
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Anticipated or actual start date
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None

Conflicts of interest
None known

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English

Country
Egypt

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
Arthritis, Rheumatoid; Humans; Probiotics

Stage of review
Ongoing

Date of registration in PROSPERO
18 February 2016

Date of publication of this revision
18 February 2016

Stage of review at time of this submission	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes

Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No