EFFECT OFF COLLAGEN SUPPLEMENTATION ON OSTEOARTHRITIS SYMPTOMS: A META-ANALYSIS OF RANDOMIZED PLACEBO-CONTROLLED TRIALS.

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• I have no financial conflicts to disclose.
INTRODUCTION

Osteoarthritis (OA) is one of the most common causes of disability and a prevalent chronic disease.

• The use of collagen is growing due to the satisfactory results in the treatment of OA. However, the possible beneficial effects of collagen for the treatment of OA are currently controversial.

• The aim of the present meta-analysis was to evaluate the effect of collagen-based supplements on OA symptoms through a meta-analysis of randomized controlled trials (RCTs).
STUDY SELECTION

• Search strategy: PubMed-Medline, Scopus, and Google Scholar databases were searched for randomized placebo-controlled trials using the following search terms in titles and abstracts (also in combination with MESH terms).

• Search output: After the initial database search, we identified 114 published trials. Then, the abstracts were reviewed, and 66 articles were excluded because they did not meet the inclusion criteria.
METHODS

The selection was restricted to randomized placebo-controlled trials evaluating the effect of orally administered collagen on OA symptoms using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale and/or the Visual Analog Scale (VAS) and providing sufficient information on WOMAC index subscores and/or VAS at baseline and at the end of follow-up in each group or presenting the net change values.

• Risk of bias assessment:
A systematic assessment of bias in the included studies was performed using the Cochrane criteria.
METHODS

• Meta-analysis was conducted using a random-effects model (using the DerSimonian-Laird method) and the generic inverse variance method. Effect sizes were expressed as weighted mean difference (WMD) and 95% CI. Heterogeneity was tested using the I² statistic index.

• Data were pooled from five RCTs comprising a total of 519 subjects, including 277 and 242 participants in the collagen treatment and placebo arms, respectively. Included studies were published between 2009 and 2016. The clinical trials used different types and/or doses of collagen. The range of intervention periods was from ten to 48 weeks. All selected trials were parallel study design. All included studies enrolled subjects affected with OA.

• The WOMAC questionnaire was originally developed to measure symptoms and physical disability of patients with OA. The measure was developed to evaluate clinically relevant changes in health status of patients as a result of intervention treatment. Moreover, the VAS is one of the major methods to assess treatment efficacy in OA.
RESULTS

Effect of collagen supplementation on OA symptoms:

• Collagen treatment showed a significant reduction in the Score of total WOMAC index (WMD = -8.00; 95% CI = -13.04, -2.95; p = 0.002).

• Stiffness subscore (WMD = 0.41; 95% CI = 0.74, -0.08; p = 0.01).

• Forest plot displaying weighted mean difference and 95% confidence intervals for the impact of collagen supplementation on total WOMAC index.
RESULTS

- Finally, a significant reduction was found in the VAS score after collagen administration (WMD = -16.57; 95% CI = -26.24, -6.89; p < 0.001.

- Forest plot displaying weighted mean difference and 95% confidence intervals for the impact of collagen supplementation on the VAS score.
STIFFNESS

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Collagen Mean [Likert]</th>
<th>Collagen SD [Likert]</th>
<th>Total</th>
<th>Placebo Mean [Likert]</th>
<th>Placebo SD [Likert]</th>
<th>Total</th>
<th>Mean Difference IV, Random, 95% CI [Likert]</th>
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</thead>
<tbody>
<tr>
<td>Benito-Ruiz 2009</td>
<td>-1.8</td>
<td>1.8</td>
<td>111</td>
<td>-1.8</td>
<td>1.5</td>
<td>96</td>
<td>26.3%</td>
</tr>
<tr>
<td>Lugo 2015</td>
<td>-3.2</td>
<td>0.7</td>
<td>54</td>
<td>-2.6</td>
<td>0.7</td>
<td>53</td>
<td>43.4%</td>
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<tr>
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<td>-0.6</td>
<td>1.5</td>
<td>15</td>
<td>10.1%</td>
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<tr>
<td>Schauss 2012</td>
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<td>1.4</td>
<td>35</td>
<td>-1.3</td>
<td>1.3</td>
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<td>18.2%</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>215</td>
<td></td>
<td></td>
<td>197</td>
<td>100.0%</td>
<td></td>
<td>-0.41 [-0.74, -0.08]</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.06; Chi² = 5.19, df = 3 (P = 0.16); I² = 42%
Test for overall effect: Z = 2.47 (P = 0.01)

Forest plot displaying weighted mean difference and 95% confidence intervals for the impact of collagen supplementation on the WOMAC Pain, Stiffness, and Functional limitation subscores.

PAIN

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Collagen supplement Mean [Likert]</th>
<th>Collagen supplement SD [Likert]</th>
<th>Total</th>
<th>Placebo Mean [Likert]</th>
<th>Placebo SD [Likert]</th>
<th>Total</th>
<th>Mean Difference IV, Random, 95% CI [Likert]</th>
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<tbody>
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<td>-4.9</td>
<td>3.5</td>
<td>111</td>
<td>-3.8</td>
<td>3.4</td>
<td>96</td>
<td>27.6%</td>
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<tr>
<td>Lugo 2016</td>
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<td>54</td>
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<td>2.2</td>
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<td>-1.9</td>
<td>3</td>
<td>15</td>
<td>18.7%</td>
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<tr>
<td>Schauss 2012</td>
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<td>2.9</td>
<td>35</td>
<td>-3</td>
<td>2.7</td>
<td>33</td>
<td>24.4%</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>215</td>
<td></td>
<td></td>
<td>197</td>
<td>100.0%</td>
<td></td>
<td>-0.22 [-1.58, 1.13]</td>
</tr>
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</table>

Heterogeneity: Tau² = 1.50; Chi² = 17.30, df = 3 (P = 0.0006); I² = 83%
Test for overall effect: Z = 0.32 (P = 0.75)
DISCUSSION

• Results of the present meta-analysis suggest that the administration of oral collagen decreases the symptoms of OA. This finding was supported by the reduction in both the total WOMAC index and VAS score.

• Hydrolyzed collagen may induce cartilage regeneration by increasing the synthesis of macromolecules in the extracellular matrix.

• Undenatured type II collagen has been described to influence the humoral and cellular immune response, protecting against the onset of joint damage through the induction and migration of T regulatory cells, also may also stimulate chondrocytes to synthetize cartilage matrix components via anti-inflammatory cytokines.

• The measure was developed to evaluate clinically relevant changes in health status of patients as a result of intervention treatment.

• Moreover, the VAS is one of the major methods to assess treatment efficacy in OA. Thus, the clinical utility of both WOMAC and VAS scales makes them the most widely used tools for the evaluation of the effectiveness of new treatments or approaches in clinical orthopaedics.
CONCLUSION

• The results of this meta-analysis showed that collagen is effective in improving OA symptoms by the decrease of both total WOMAC index and VAS scale.

• Nevertheless, further longer clinical trials in larger populations are required in order to corroborate the potential beneficial effects of collagen supplementation in patients with symptomatic OA.
REFERENCES


