Silymarin effect on persistent allergic Rhinitis

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Introduction

- In the wide range of allergic diseases, **allergic rhinitis** with a **20% prevalence** rate is the most common type.

- Its financial costs and major influence on life quality are substantial.
Manifestation

• Typically, allergic rhinitis is caused by natural pollens or house-dust mites.
• Symptoms:
  ✓ Runny nose
  ✓ Nasal itching
  ✓ Sneezing
  ✓ Nasal congestion
  ✓ Conjunctivitis
  ✓ Smelling disorder
Allergic Rhinitis

- **Persistent**: Symptoms present > 4 days a week and > 4 consecutive weeks

- **Intermittent**: Symptoms present < 4 days a week or < 4 consecutive weeks
AR Management

- During the recent years significant changes have occurred in the management of allergic rhinitis.

- The role of oxidants and oxidative stresses in the pathophysiology of allergic rhinitis has been confirmed in several studies.
Silymarin

- Silymarin is a polyphenolic flavonoid derived from milk thistle (Silybum marianum) with well-proven hepato-protective effects
Geographic Distribution

- Milk thistle is a spiny European plant which is commonly found in North America.
History

- Its products have been in practice for over 200 years & it has been widely used clinically since 1969 in European countries.

- Silymarin is absorbed in the intestine and is concentrated in the biliary system followed by the hepatic cycle.
Properties

- It has several effects including:
  - Anti-inflammatory
  - Antioxidant
  - Cytoprotective
  - Anticarcinogenic
Mechanism

- How silymarin produces these effects is not understood.
- It may involve suppression of NF-κB, a nuclear transcription factor, which regulates the expression of various genes involved in inflammation, cytoprotection, and carcinogenesis.
Clinical Usage

Recent studies have shown that silymarin also has other properties such as therapeutic effects on:

- Fatty liver
- Hepatic cirrhosis
- Diabetes
- Hyperlipidemia
- Cataract
- Osteoporosis
- Cancer
Adverse effects

- Reports of adverse events while receiving silymarin therapy are rare.

- Nausea
- Epigastric discomfort
- Arthralgia
- Pruritus
- Headache
- Urticaria
Hypothesis

- Although during the past decade silymarin has been used as a strong antioxidant in various studies and different diseases including cardiovascular disease, diabetes, cancers, toxic and alcoholic hepatitis, etc, it has not yet been applied in allergic rhinitis.
PATIENTS AND METHODS
Study Design

- **Randomized clinical trial** which evaluates the added effect of silymarin on controlling the signs and symptoms of allergic rhinitis.

- In addition, some **Cytokines, Serum IgE level, Nasal Eosinophil** were determined.
Patients

- 60 out of 109 patients with persistent allergic rhinitis who visited the allergy or ear, nose and throat (ENT) clinic of Qaem educational hospital, Mashad, Iran, from May 2009 through January 2010 were randomly selected.
Clinical Assessment

- After filling a written informed consent, the patients' symptoms were recorded based on the standard SN O T-20 questionnaire.
- Afterwards and by a single physician the patients were randomly and in a double blind manner divided into the study and control groups.
Lab Assessment

- A skin test for all the common regional aeroallergens was also obtained from each case in order to confirm the allergic base of the disease.
- The percentage of eosinophils on nasal smear was then measured under a high power field microscope.
- Serum IgE and cytokines (IL-4, 5 and IFN-γ) were also quantified.
Groups

- The cases were divided into two groups:
  - **Case Group:** Silymarin was administered
  - **Control group:** was treated with placebo.
• Besides continuing the routine modalities for allergic rhinitis in both groups, a one-month treatment course of silymarin with a dosage of 140mg three times daily was administered for the study group.

• The control group received placebo with the same packing, dosage and for the same duration.
Exclusion Cr

- Patients with:
  - Any other etiology for rhinitis
  - Other related systemic diseases
  - Those taking any kind of herbal drug
  - Drugs with anti oxidant or anti inflammatory effects
  - Who showed drug side effect
RESULTS
Demography

- No significant difference in age and sex was seen between the two groups.
- 12 (40%) patients and 11 (36.7%) controls were males.
- Mean age of the study and control groups were 29.03 ± 10.17yrs and 28.4 ± 8.41yrs, respectively.
## Study group

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>After</th>
<th>T-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom severity (SNOT)</td>
<td>23.5 ± 8.05</td>
<td>14.27 ± 5.99</td>
<td>&lt; 0.001</td>
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<tr>
<td>Nasal smear eosinophil (%)</td>
<td>17.43 ± 29.7</td>
<td>18.32 ± 30.9</td>
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<td>Serum IgE level</td>
<td>796.8 ± 637.95</td>
<td>1399.3 ± 1305.7</td>
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<td>Serum IL-4 level</td>
<td>12.5 ± 11.18</td>
<td>10.79 ± 13.11</td>
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<td>Serum IL-5 level</td>
<td>5.36 ± 5.01</td>
<td>4.65 ± 5.04</td>
<td>0.554</td>
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<tr>
<td>Serum IFN-γ level</td>
<td>306.28 ± 124.8</td>
<td>296.76 ± 183.3</td>
<td>0.810</td>
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</table>
## Control Group

<table>
<thead>
<tr>
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<th>T-test</th>
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<tbody>
<tr>
<td>Symptom severity (SNOT)</td>
<td>20.0 ± 8.75</td>
<td>17.8 ± 7.99</td>
<td>&lt; 0.001</td>
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<td>Nasal smear eosinophil (%)</td>
<td>16.59 ± 28.58</td>
<td>18.2 ± 29.7</td>
<td>0.683</td>
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<tr>
<td>Serum IgE level</td>
<td>1232.15 ± 1454.5</td>
<td>1228 ± 1689.7</td>
<td>0.984</td>
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<tr>
<td>Serum IL-4 level</td>
<td>7.24 ± 11.77</td>
<td>9.36 ± 10.63</td>
<td>0.401</td>
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<td>Serum IL-5 level</td>
<td>3.95 ± 4.87</td>
<td>5.42 ± 4.95</td>
<td>0.236</td>
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<td>Serum IFN-γ level</td>
<td>247.28 ± 155.88</td>
<td>238.2 ± 164.48</td>
<td>0.824</td>
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<td></td>
<td>Study group</td>
<td>Control group</td>
<td>T-test</td>
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<tr>
<td><strong>Symptom severity (SNOT)</strong></td>
<td>9.23 ± 5.14</td>
<td>2.2 ± 2.69</td>
<td>&lt;0.001</td>
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<tr>
<td><strong>Nasal smear eosinophil (%)</strong></td>
<td>-0.89 ± 38.2</td>
<td>-1.62 ± 21.18</td>
<td>0.929</td>
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<tr>
<td><strong>Difference in Pre- &amp; post-treatment serum IgE level</strong></td>
<td>-602.5 ± 1004.6</td>
<td>3.8 ± 1004.9</td>
<td>0.027</td>
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<td><strong>Difference in Pre- &amp; post-treatment IFN-γ level</strong></td>
<td>9.52 ± 211.8</td>
<td>9.08 ± 213.3</td>
<td>0.993</td>
</tr>
<tr>
<td><strong>Difference in Pre- &amp; post-treatment IL-4 level</strong></td>
<td>1.71 ± 15.93</td>
<td>-2.12 ± 13.17</td>
<td>0.327</td>
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<td><strong>Difference in Pre- &amp; post-treatment IL-5 level</strong></td>
<td>0.7 ± 6.29</td>
<td>-1.47 ± 6.42</td>
<td>0.202</td>
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DISCUSSION
CLINICAL EFFECTS
Clinical Presentation

- The dominant symptoms of allergic rhinitis were also recorded in these patients which similar to previous studies mainly included nasal congestion, clear watery rhinorrhea and sneezing.
Clinical effects

- Showed a significant improvement in the severity of clinical symptoms based on the Sino Nasal Outcome Test (SNOT-20)
• Other herbal products with confirmed antioxidant and anti-inflammatory effects have been examined in this disease and a desired outcome mostly in relieving major symptoms and improving the quality of life of such patients has been achieved.
• In numerous studies herbal mixtures (e.g. Aller-7) have been used in treating allergic rhinitis.

• A significant improvement has been observed in major symptoms, life quality, total eosinophil count.
Saxena et al reported a significant decrease in the total eosinophil count after treatment with an herbal mixture of Aller 7 with antioxidan properties.
Although the role of antioxidants and oxidative stresses has been proved in several studies, no study has yet been performed on the effect of silymarin (with the proven antioxidant effect) in the treatment of allergic rhinitis.
LAB EFFECTS
Nasal Eosinophilia

- In our study the post-treatment nasal smear eosinophil percentage showed a significant difference in neither groups nor between the two (p>0.1).
- However, nasal smear eosinophil percentage is not a reliable variable in diagnosis or treatment follow-up of allergic rhinitis.
Serum IgE

- Serum IgE level showed a significant rise after treatment with silymarin whereas regarding the effect of silymarin, it was supposed to decrease.
- Considering that the diseases symptoms had markedly improved in cases in comparison to controls, the rise in IgE level could also be defined as a probable allergic reaction to the drug.
Cytokines

- We expect that **IL-5** (eosinophils accumulation) and **IL-4** (the main Th2 cells cytokine decrease due to effective treatment of allergic rhinitis and at the same time **IFN-γ**, (the main cytokine of Th1 cells) increase.

- Non-changing condition in cytokine levels after silymarin treatment could the result of inefficiency of this drug particularly on the laboratory and immunologic findings of this disease.
Oxidative

- Perhaps Oxidative stress indexes might have shown changes if were determined
CONCLUSION
• Considering silymarin as a safe medicinal plant that alleviates the severity of clinical symptoms in allergic rhinitis with high rate of patient satisfaction; more study on the exact effect of it on AR and clinical usage highly recommended.
THANK YOU FOR YOUR ATTENTION