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Treatment of bronchial asthma with an aqueous extract of Mangifera indica L. (VIMANG®): two cases report

Abstract

A case report was carried out in two asthmatic patients treated with a new health natural product named Vimang®, an aqueous extract of Mangifera indica L. stem bark, which has been registered as antioxidant and anti-inflammatory. A 39 years-old female with persistent moderate asthma and a 43 years-old male with persistent severe asthma were treated orally with Vimang® (capsule 300 mg, one every 8 h) during three months. Respiratory functional tests and determination of total serum immunoglobulin E (IgE), eosinophil cationic protein (ECP) and metalloproteinase-9 (MMP-9) activity were done at times 0, 6 and 12 weeks, respectively. An improvement in the volume of force expiration (FEV1) was observed for both patients. The values of IgE, ECP and the enzymatic activity of MMP-9 decreased also for both patients. These results could open the way to further clinical researches about the use of Vimang® as an alternative for the treatment of bronchial asthma.

Keywords: Mangifera indica; Vimang; Asthma; IgE; Eosinophil cationic protein; Force expiration volume.

Resumen

Un reporte de caso fue realizado en dos pacientes asmáticos tratados con un nuevo producto natural de salud llamado Vimang®, un extracto acuoso de la corteza de Mangifera indica L. que ha sido registrado como antioxidante y antiinflamatorio. Una mujer de 39 años con asma moderada persistente y un hombre de 43 años con asma severa persistente fueron tratados por vía oral con Vimang® (cápsulas 300 mg, una cada ocho horas durante tres meses). En las semanas 0, 6 y 12 se realizaron pruebas funcionales respiratorias y determinaciones de inmunoglobulina E total en suero (IgE), proteína catiónica de eosinófilo (ECP) y la actividad de metaloproteinasa-9 (MMP-9). En ambos pacientes se observó una mejoría en el volumen de espiración forzada (FEV1). Los valores de IgE, ECP y la actividad de MMP-9 decrecieron en ambos pacientes. Estos resultados podrían sentar las bases para la realización de más investigaciones clínicas acerca del uso del Vimang® como una alternativa para el tratamiento del asma bronquial.

Palabras Clave: Mangifera indica; Vimang; Asma; IgE; Proteína catiónica de eosinófilo; Volumen espiratorio forzado.
INTRODUCTION

Vimang® is the brand name of formulations from an aqueous extract of the stem bark of selected varieties of *Mangifera indica* L. (Anacardiaceae) traditionally used in Cuba for its anti-inflammatory, analgesic, antioxidant and immunomodulatory properties (Garrido et al., 2007). Chemical studies performed with this extract have enabled the isolation and identification of phenolic acids, phenolic esters, flavan-3-ols, mangiferin, which is the predominant component of this extract, and micronutrients as selenium (Nuñez-Sellés et al., 2002). Also, acute and chronic toxicology studied have demonstrated the safety of the extract (Gámez et al., 2002).

Recently, it was demonstrated Vimang® has antiallergic properties through the inhibition of IgE production, histamine release from rat mast cells and lymphocyte proliferative response (Rivera et al., 2006). Also, Vimang® reduces eosinophil migration into bronchoalveolar space and peritoneal cavity, and eosinophil generation in bone marrow and blood during an asthma murine model. This reduction was associated with inhibition of IL-5 production in serum and eotaxin in lung homogenates (Sa-Nunes, et al., 2006).

According to these experimental evidences, the aim of the present investigation was to describe the effects of Vimang® in the treatment of two patients with different asthma severity.

MATERIALS AND METHODS

Cases presentation

Two asthmatic patients were chosen. The patients were classified according to the Global Strategy for Asthma Management and Prevention (GINA, 2006). Their clinical conditions were as follow:

**Persistent Moderated Asthmatic Patient:** 39 years-old female. Standard treatment: salmeterol and fluticasone spray (Seretide® 25/50 µg) 3 puffs daily. Allergic potential: presence of animals, dust and perfumes. Symptoms included dry coughing and breath shortening.

**Persistent Severe Asthmatic Patient:** 43 years-old male. Standard treatment: salmeterol and fluticasone spray (Seretide® 25/50 µg) 3 puffs daily. Allergic potential: dust. Symptoms included repetitive breath shortening and pronounced dry coughing.

Capsules: Vimang® capsules were prepared with 300 mg of dry extract obtained from a standard *Mangifera indica* L. stem bark. This extract was prepared by decoction with water for 1 h and then it was concentrated by evaporation and spray-dried to obtain a fine homogeneous brown powder with a particle size of 30–60 mm. (Nuñez-Sellés et al 2002). The lot used in the study was 200402-E from Novatec Laboratory (La Habana, Cuba). The quality control analysis showed more than 50% of total polyphenols, according to the established specification.

Both patients received one capsule of Vimang®, 300 mg, every 8 h, during 3 months. Respiratory functional tests were done to both patients at times 0, 6 and 12 weeks of treatment as described. Blood samples were collected and the serum was obtained and stored at -20 ºC until the determination of IgE, ECP and MMP-9.

Experimental methods

**Measurement of the Force Expiration Volume in one second (FEV1):** Measurement of FEV1 was done using computerized spirometers (Modular Collins G.S., USA). The treatment was considered beneficial when FEV1 values pre- and post-aerosol improved equal or superior than 10% compared to 0, 6 and 12 weeks of treatment.

**Determination of serum total IgE and ECP:** ECP and IgE concentrations were measured by an immunofluorescence ELISA technique according with the manufacturer instructions (ImmunoCAP, Pharmacia-Upjohn, USA).

**Determination of enzymatic activity of MMP-9:** The enzymatic activity of MMP-9 in blood serum was determined by gelatin zymographs (Atkinson and Senior, 2003). Briefly, each serum sample was diluted (1:10) and subjected to electrophoresis on 10% polyacrylamide SDS gels containing 1 mg/ml of porcine skin gelatin (Sigma, USA). Gelatin digestion was identified as clear zones of lysis against a blue background. Molecular weights of gelatinolytic bands were estimated using SDS-polyacrylamide gel electrophoresis (PAGE) protein standards. Gelatinolytic activity was measured on zymography-digitized images (Bioimaging System, Syngen, Canada).

Both patients were informed about the treatment and they gave written informed consent to be included in the study. The Ethics Committee of CIMEQ Hospital (La Habana, Cuba) approved the study, and it
was carried out in accordance with the current good clinical practice guidelines (GCP).

RESULTS

Serum concentrations of total IgE and ECP were reduced and FEV1 values were improved in both patients after Vimang® treatment (Table 1). MMP-9 activity in blood serum was also reduced (Fig. 1).

Table 1. Blood serum concentrations of IgE and ECP, MMP-9 activity and FEV1 values in asthmatic patients after Vimang® treatment.

<table>
<thead>
<tr>
<th>Time (weeks)</th>
<th>IgE (kU/l)</th>
<th>ECP (ng/ml)</th>
<th>Pre</th>
<th>Chg (%)</th>
<th>Post</th>
<th>Chg (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Persistent moderated asthmatic patient</td>
<td></td>
<td></td>
<td>0</td>
<td>1369</td>
<td>51.6</td>
<td>1.75</td>
</tr>
<tr>
<td>6</td>
<td>1174</td>
<td>40.4</td>
<td>2.23*</td>
<td>27</td>
<td>2.10</td>
<td>18</td>
</tr>
<tr>
<td>12</td>
<td>740</td>
<td>29.8</td>
<td>2.62*</td>
<td>50</td>
<td>2.23</td>
<td>25</td>
</tr>
<tr>
<td>B. Persistent severe asthmatic patient</td>
<td></td>
<td></td>
<td>0</td>
<td>422</td>
<td>62.9</td>
<td>2.16</td>
</tr>
<tr>
<td>6</td>
<td>368</td>
<td>41.8</td>
<td>2.39*</td>
<td>11</td>
<td>2.49</td>
<td>0</td>
</tr>
<tr>
<td>12</td>
<td>290</td>
<td>30.7</td>
<td>2.62*</td>
<td>21</td>
<td>2.74</td>
<td>10</td>
</tr>
</tbody>
</table>

* Represents the improvement of patients FEV1 with respect to the initial values. Chg- Change respect time 0. Pre and Post- values pre- and post-aerosol improved equal or superior than 10% compared to 0, 6 and 12 weeks of treatment.

Figure 1. MMP-9 activity (gelatinase) in blood serum of asthmatic patients after Vimang® treatment during three months, determined by Zymography using sera of both patients.

Lane S: protein standard, kD (inserted); Lane 1, 2, 3: persistent moderated asthmatic patient at time 0, 6 and 12 weeks, respectively; Lane 4, 5, 6: persistent severe asthmatic patient at time 0, 6 and 12 weeks, respectively.

The patient with persistent moderated asthma did not show any of the allergic symptoms as above described (to see Materials and Methods) during the 3 months of treatment with Vimang® capsules. Any other drug was administered during the study. On the other hand, the patient with persistent severe asthma didn’t have acute symptoms during the treatment and he took only salbutamol at the second and fifth weeks, one time each. Significantly, the steroids never were consumed by neither the two patients during the three months of treatment. No adverse events were reported during the treatment.

DISCUSSION

In this study it was found that the treatment with Vimang® capsules (300 mg, orally, every 8 h during 3 months) of two patients with persistent moderated and persistent severe asthma improved the measured values of FEV1, IgE, ECP and MMP-9.

IgE, ECP and MMP-9 are important mediators involved in the physiopathology of bronchial asthma. IgE is the most important antibody implicated in this disease and some studies have shown the local production of IgE in allergic airway diseases (Smurthwaite and Durham, 2002). The activation of eosinophils gives rise to the extracellular release of a number of potent cytotoxic proteins such as ECP, which have been associated with the development of subacute and chronic symptoms of allergy (Venge, 2004). MMP-9 (gelatinase B, 92-kDa gelatinase) induces the migration of eosinophils, lymphocytes, neutrophils, dendritic cells and the deposition and degradation matrix (Atkinson and Senior 2003; Kelly and Jarjour, 2003).

Experimental studies in mice have demonstrated the capacity of Vimang® to reduce IgE and IL-5 production, and the maturation and migration of eosinophils (Rivera et al., 2006; Sa-Nunes et al., 2006), which support the described clinical results. Also, Vimang® has about 50% of polyphenols in its composition, and they are reported that possess in vivo anti-allergic activity (Cheong et al., 1998).

Recently, some evidences suggested that oxidative chemical species produced by the airway inflammatory cells plays an essential role in the pathogenesis of bronchial asthma. These results are in correspondence with other studies in which they have been utilized as alternative medicine products such as TJ-96 and Pycnogenol® (Nadeem et al., 2003). It has been also evidenced that the antioxidant endogenous capacity is decreased in asthmatic patients. Therefore, Vimang®, which has shown a high antioxidant capacity besides its anti-inflammatory effects (Martínez et al., 2000; Garrido et al., 2007), could be
an alternative or complementary antioxidant therapy for the treatment of asthmatic patients.

**CONCLUSION**

Both asthmatic patients included in this study reduced the total IgE and ECP concentrations, and MMP-9 activity in blood serum and improved the respiratory function (FEV1) after treatment with Vimang® capsules during 3 months avoiding the use of steroids. These evidences could open the way to further clinical trials about the use of Vimang® as an alternative or complementary therapy for the treatment of bronchial asthma.

**ACKNOWLEDGEMENTS**

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