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File: ■ Pomegranate (*Punica granatum*, Lythraceae)
■ Lung Function
■ Allergic Asthma

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RE: Pomegranate Extract May Improve Lung Function Parameters in Adults with Persistent Mild to Moderate Asthma

Shateri Z, Hosseini SA, Abolnezhadian F, Maraghi E, Shoushtari MH, Zilae M. Pomegranate extract supplementation improves lung function parameters and IL-35 expression in participants with mild and moderate persistent allergic asthma: A randomized, double-blind, placebo-controlled trial. *Front Nutr.* October 18, 2022;9:1026343. doi: 10.3389/fnut.2022.1026343.

One of the most common chronic respiratory ailments, asthma affects > 300 million people globally. Inflammation, increased airway responsiveness and remodeling, excess mucus production, and reversible airway obstruction are its prominent features. Incidence of asthma is rising worldwide, likely due to environmental alterations of industrialization. Incidence of asthma in Iran, from 5-15%, is higher than global and regional averages with some Iranian cities experiencing more than twice the national average per capita. Existing treatments are associated with adverse effects and limitations. Dietary polyphenols exert antioxidant and anti-inflammatory effects. Pomegranate (*Punica granatum*, Lythraceae) fruit is rich in ellagic acid, a polyphenol that has reduced inflammatory markers in clinical trials in patients with diabetes and with rheumatoid arthritis. These authors conducted a randomized, double-blind, placebo-controlled clinical trial (RCT) to determine the impact of a pomegranate extract on lung function parameters in patients with mild to moderate asthma.

Patients were recruited at an asthma and allergy clinic in Ahvaz, Khuzestan Province, Iran, an asthma hot spot. A total of 70 participants were enrolled in the two-arm, parallel group RCT. Eligible patients were aged 18-65 years with persistent mild or moderate asthma, immunoglobulin-E \geq 30 IU, and body mass index > 30 kg/m². Patients who were pregnant/lactating or smokers, who had taken mineral or multivitamin supplements in the previous two months or were taking any medicines other than for asthma, and those with malignancy, diabetes, or other pulmonary or autoimmune disease were excluded.

Asthma severity and response to treatment was assessed via pro-oxidant/antioxidant balance (PAB), serum levels of high-sensitivity C-reactive protein (hs-CRP) and interleukin (IL)-35, and spirometry. Participants were stratified as having mild or moderate asthma based on spirometric results for forced expiratory volume in one

second (FEV₁) and clinical symptoms using Global Initiative on Asthma diagnostic criteria. Half of the participants had mild asthma and half, moderate; evenly divided between groups. Female-identifying participants comprised 57.81% of the sample. At baseline and eight weeks, venous blood samples were collected, and spirometry tests were administered. At baseline, there were no statistically significant ($P < 0.05$) between-group differences in dietary or anthropometric values, asthma severity, physical activity, clinical features, types of medicines used, or age of asthma onset. Participants were asked not to alter their physical activity or energy intake during the RCT. Physical activity was evaluated using an international questionnaire at baseline and eight weeks. Patients were asked not to consume pomegranate products during the RCT, to avoid foods to which they were allergic and processed foods, and to refrain from taking dietary supplements. At baseline and eight weeks, they completed 24 h dietary recalls for three days. The study physician prescribed similar asthma drugs to patients. They were asked not to use bronchodilators before spirometry.

Matching capsules of pomegranate extract and placebo (melba toast, ingredients not stated) were prepared by the Institute of Medicinal Plants (Karaj, Alborz Province, Iran). Pomegranate capsules contained 250 mg seed extract, 2.1 μg ellagic acid, 118.4 μg punicalagin- α , and 53 μg punicalagin- β as per high-performance liquid chromatography. Participants took two capsules/d for eight weeks. There were three dropouts in each group for a final cohort of 64. At eight weeks, there was no statistically significant between-group difference in IL-35 levels ($P = 0.172$), but a significant increase was seen in the pomegranate group ($P = 0.031$), with a significant difference between groups in change levels ($P = 0.026$). There were no significant between-group differences in hs-CRP or PAB levels at eight weeks. Subgroup analysis found changes in IL-35 significant only in the pomegranate group with mild asthma ($P = 0.03$) and change levels between groups significant only when comparing patients with mild asthma ($P = 0.02$). Subgroup analysis found no between-group differences in hs-CRP or PAB regardless of asthma severity.

Spirometry at eight weeks revealed improved forced expiratory flow 25-75% for pomegranate vs. baseline ($P = 0.012$), improved FEV₁/forced vital capacity ratio (FVC; $P = 0.001$), and improved FEV₁ ($P = 0.031$). The improved FEV₁/FVC ratio was significant between groups ($P = 0.028$), as were change levels in this ratio ($P = 0.023$). In subgroup analysis, these changes were significant only in pomegranate group patients with mild asthma. Compared to those with mild asthma in the placebo group, the change in FEV₁/FVC ratio was significant ($P = 0.008$). Pomegranate group patients with moderate asthma had significant improvements in FEV₁ and FEV₁/FVC ratio ($P = 0.03$; $P = 0.02$, respectively), but there were no significant between-group differences in spirometric measures in moderate asthma ($P > 0.05$).

Future studies should examine additional inflammatory markers and be of longer duration. The authors report no conflicts of interest.

—*Mariann Garner-Wizard*

Referenced article can be accessed at <https://www.frontiersin.org/articles/10.3389/fnut.2022.1026343/full>.