High-Dose Oral Garlic is Associated with a Decrease in Intrapulmonary Shunting in Severe Hepatopulmonary Syndrome

TO THE EDITOR:

Hepatopulmonary syndrome (HPS) is characterized by pathological vasodilation of the pulmonary vasculature that results in an arterial oxygenation defect in patients with liver disease. These intrapulmonary vasodilations are mediated by vasoactive molecules, such as endothelin-1 and nitric oxide. The result is both ventilation-perfusion mismatch and impaired oxygen diffusion, causing a "shunt" of poorly oxygenated blood to the systemic circulation. Clinically, this causes dyspnea and hypoxia, particularly when standing, known as platypnea and orthodeoxia. The diagnosis of HPS is made by demonstrating that the patient with liver disease has a partial pressure of arterial oxygen (PaO₂) <80 mm Hg or an A-a gradient >15 mm Hg, as well as an intrapulmonary shunt on a transthoracic contrast-enhanced echocardiogram (TTCE).

HPS severity is classified according to the degree of hypoxemia, and the contribution of HPS-induced hypoxemia can be quantified on technetium-9 mm macroaggregated albumin (MAA) scanning. (1) In this scan, labeled biodegradable particles are delivered intravenously and normally become trapped in lung capillaries. However, in HPS they bypass the lungs and become detectable in other organs, such as the brain.

Ultimately, patients with HPS have increased mortality from liver disease, and prognosis worsens with increasing severity. Currently, the only cure is liver transplantation. Supplemental oxygen can be used to palliate symptoms. While medical therapies remain limited, there are some data to support the use of oral garlic supplementation. (2,3) In a randomized placebo-controlled trial, patients with HPS who received high-dose garlic (1-2 mg/m²) had a greater increase in PaO_2 (24.66% vs. 7.37%; P < 00.1). (3)

We are writing to describe the use of high-dose oral garlic in a patient with newly diagnosed severe HPS undergoing assessment for liver transplantation. This 67-year-old woman had Child-Pugh-B7

cirrhosis secondary to nonalcoholic steatohepatitis and presented with dyspnea. She had marked orthodeoxia on room air $(PaO_2, 97 \text{ mm Hg lying and } 42 \text{ mm Hg standing})$ and an intrapulmonary shunt on TTCE, quantified to be 38% on MAA scanning (normal <6%). She opted to try Kyolic Aged Garlic Extract 2 g daily, based on its positive trial. $^{(3)}$

After three weeks, her dyspnea had decreased and her only adverse reaction was mild halitosis. Her arterial blood gases (Table 1) showed an increase in oxygenation not attributable to hyperventilation. She underwent MAA scanning to reassess her intrapulmonary shunt (Fig. 1), which had decreased to 32.5% (relative reduction, 14.5%; absolute reduction, 5.5%). She was subsequently waitlisted for transplantation and discharged on home oxygen.

This is the first case quantifying the reduction in intrapulmonary shunting associated with high-dose garlic for HPS.

TABLE 1, ARTERIAL BLOOD GAS ANALYSIS AT ADMISSION TO HOSPITAL AND 3 WEEKS AFTER GARLIC THERAPY*

Date	April 9, 2018	May 2, 2018	Normal Range
рН	7.48	7.43	7.38-7.42
PaO_2 (mm Hg)	<u>42</u> †	<u>47</u>	85-105
pCO ₂ (mm Hg)	<u>29</u>	<u>29</u>	35-45
HCO ₃ (mmol/L)	<u>21</u>	<u>19</u>	85-100
SaO ₂ (%)	<u>78.3</u>	<u>79</u>	95-98
Sodium (mmol/L)	139	135	138-142
Potassium (mmol/L)	4	3.5	3.8-5.0
Chloride (mmol/L)	<u>113</u>	<u>111</u>	95-110
Calcium ionized (mmol/L)	1.06	1.19	1.15-1.29
Hemoglobin (g/L)	102	<u>106</u>	130-180
Oxyhemoglobin (%)	<u>76.7</u>	<u>77.3</u>	94-97
Carboxyhemoglobin (%)	<u>1.8</u>	<u>1.7</u>	0-1.5
Methemoglobin (%)	0.2	1.0	0-1.5
Glucose (mmol/L)	<u>12.1</u>	10.8	4.0-7.8
Lactate (mmol/L)	Not available	<u>2.5</u>	0.5-2.0

*Taken on room air while standing.

[†]Underlined numbers indicate abnormal results.

Abbreviations: pCO_2 , partial pressure of carbon dioxide; SaO_2 , oxygen saturation.

99m Tc MAA Hepatopulmonary Shunt POSTERIOR CHEST ANTERIOR CHEST LT LATERAL BRAIN В 99mTc-MAA Hepatopulmonary Shunt Study ROI Analysis Posterior Lungs Lt Lateral Brain

FIG. 1. The MAA scans above were performed prior to (A, above) and post (B, below) garlic therapy. The reduction in intrapulmonary shunting associated with garlic therapy is demonstrated by the increased opacity of the lung fields in scan B, compared to scan A.

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REFERENCES

 Fragaki M, Sifaki-Pistolla D, Samonakis DN, Koulentaki M, Koukouraki S, Stathaki M, et al. Screening for hepatopulmonary syndrome in cirrhotic patients using technetium 99m-macroaggregated albumin perfusion lung scan (Tc-MAA): diagnostic approach and clinical correlations. J Clin Gastroenterol 2018;52:828-834.

- Abrams GA, Fallon MB. Treatment of hepatopulmonary syndrome with *Allium sativum* L. (garlic): a pilot trial. J Clin Gastroenterol 1998;27:232-235.
- 3) De BK, Dutta D, Pal SK, Gangopadhyay S, Das Baksi S, Pani A. The role of garlic in hepatopulmonary syndrome: a randomized controlled trial. Can J Gastroenterol 2010;24:183-188.
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DOI 10.1002/hep4.1432

Potential conflict of interest: Nothing to report.