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File: ■ Jimson Weed (*Datura stramonium*, Solanaceae)
■ Rhubarb (*Rheum palmatum* Polygonaceae)
■ Ginger (*Zingiber officinale*, Zingiberaceae)
■ Acacia (*Acacia senegal* syn. *Sengalia senegal*, Fabaceae)
■ Hab-o Shefa
■ Opioid Dependence

HC 052032-656

Date: January 15, 2021

RE: Herbal Combination Hab-o Shefa May Improve Relapse Rates and Feelings of Craving, Anxiety, and Depression in Patients with Opioid Use Disorder

Moosavyzadeh A, Mokri A, Ghaffari F, et al. Hab-o Shefa, a Persian medicine compound for maintenance treatment of opioid dependence: randomized placebo-controlled clinical trial. *J Altern Complement Med*. May 2020;26(5):376-383. doi: 10.1089/acm.2019.0390.

Treating opioid dependence involves reducing withdrawal symptoms, controlling craving, stopping the rewarding effects of drugs, and treating comorbidities such as depression and anxiety. In many countries, traditional medicines are used to treat addiction. In Iranian medicine, the herbal combination Hab-o Shefa has been studied for its use in treating opiate addiction. Hab-o Shefa contains 43.3% jimson weed (thorn apple; *Datura stramonium*, Solanaceae), 27.9% rhubarb (*Rheum palmatum* Polygonaceae), 14.4% ginger (*Zingiber officinale*, Zingiberaceae), and 14.4% acacia (*Acacia senegal* syn. *Sengalia senegal*, Fabaceae). These authors conducted a randomized, parallel-group, double-blind, clinical trial to investigate the preliminary effects of Hab-o Shefa on relapse, craving, anxiety, and depression in the maintenance treatment of patients with opioid use disorder.

The study was conducted from July 2015 to March 2017 and included patients at a residential center for addiction treatment in Isfahan, Iran. Eligible patients met the Diagnostic and Statistical Manual of Mental Disorders-IV criteria for addiction, were aged between 18 and 65 years, and were healthy. Of the 164 patients who were screened for eligibility, 107 patients enrolled and entered detoxification. During this time, they were given clonidine and nonsteroidal anti-inflammatory drugs for 10 to 14 days. The drugs were gradually withdrawn within a week, followed by a morphine urine test. If that test was negative, a naloxone challenge test was conducted to determine opioid dependence.

Twenty-six of the patients did not complete detoxification and were not included in the trial. Forty-one of the remaining patients were randomly assigned to the Hab-o Shefa group, and the other 40 patients made up the placebo group.

Dry plant material was purchased from Vazir Nezam Company in Tehran, Iran, and used to prepare the 500 mg Hab-o Shefa capsules. Powdered sugar was used as placebo. During the 12-week study, the patients took one capsule on the first day, two capsules on the second day, and three capsules on the third day and daily for the remainder of the study.

The patients were evaluated at baseline before treatment and at four, eight, and 12 weeks after the start of treatment. Outcome measures included the number of opioid-negative urine tests; feelings of craving, depression, and anxiety; and retention time in treatment. Vital signs and the occurrence of any adverse effects were recorded. Both groups were similar in demographic and clinical characteristics at baseline. Mean retention times were 66.6 ± 30.28 days in the Hab-o Shefa group and 59.60 ± 34.80 days in the placebo group.

In the Hab-o Shefa group, 17 patients left the residential center, one patient relapsed, and two patients had adverse effects. In the placebo group, 11 patients left the residential center, three patients relapsed, and six patients dropped out because of insufficient efficacy. Forty-one patients completed the study. The frequency of relapse rates, as indicated by positive results on the morphine urine tests, was significantly higher in the placebo group compared with the Hab-o Shefa group after week 8 ($P = 0.003$) and week 12 ($P = 0.001$). In the placebo group, the self-reported days of opioid use increased after 12 weeks compared with baseline ($P = 0.001$).

The craving rate decreased significantly in the Hab-o Shefa group compared with baseline ($P = 0.002$) and compared with the placebo group ($P = 0.001$). In the placebo group, the craving score decreased after four weeks but increased after eight and 12 weeks. Compared with the placebo, the Hab-o Shefa improved depression ($P = 0.010$) and anxiety ($P = 0.035$) scores.

Among the study's limitations are the large number of dropouts, the small sample size, the failure to follow up after the end of treatment to evaluate efficacy and possible adverse effects, and the possibility of false-negative urine morphine tests. The authors conclude that "Hab-o Shefa could be useful for opioid maintenance treatment, and it can also be considered as a new promising drug for prevention of craving and relapse."

The authors declare no conflicts of interest.

—*Shari Henson*

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