Hawthorne and the Heart: A Research Update

A number of key studies have been undertaken since my last article in this column covering the cardiovascular research for the herb Hawthorne (Crataegus monogyna or C. laevigata). Significantly, a meta-analysis was published in June 2003 that assessed the evidence from randomized, double-blind, placebo-controlled trials published to June 2002. Eight trials were selected for analysis, representing a total of 632 patients with NYHA classes I and II cardiac disease (and also class III in one trial). For more information on the NYHA classification, see Table 1. The meta-analysis concluded that Hawthorne therapy provided significant clinical benefit in terms of increased maximal cardiac workload (improved by a mean of 7 Watt), decreased pressure-rate product (indicating reduced workload for the heart), and decreased dyspnea and fatigue.

Table 1 - New York Heart Association (NYHA) Classification for Cardiac Disease

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<th>Class</th>
<th>Description</th>
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<tbody>
<tr>
<td>I</td>
<td>Patients have cardiac disease, but without the resulting limitations on physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.</td>
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<tr>
<td>II</td>
<td>Patients have cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.</td>
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<tr>
<td>III</td>
<td>Patients have cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary physical activity causes fatigue, palpitation, dyspnea, or anginal pain.</td>
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<tr>
<td>IV</td>
<td>Patients have cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency or of the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.</td>
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In ongoing studies, the effects of Hawthorne extract on several cardiovascular parameters and on cardiovascular endpoints of patients with NYHA II-III cardiac failure are under investigation. Since the extract is well tolerated, it could complete the standard treatment of chronic cardiac failure in the future. The purpose of one relatively recent study was to investigate whether long-term therapy with Hawthorne leaf and flower extract (HLFE) is efficacious as an add-on therapy to pre-existing diuretic treatment in patients with heart failure with a more advanced stage of the disease (NYHA class III); whether effects are dose-dependent; and whether the treatment is safe and well tolerated. Exercise capacity was assessed by use of seated bicycle ergometry with incremental workloads. Scores for subjective symptoms and complaints made by the patients were also analyzed. Efficacy and tolerability of the treatments were judged by both the patients and investigators. Safety was assessed by the documentation of adverse events and the safety laboratory.

A total of 209 patients were randomized to treatment with 1800 mg of HLFE, 900 mg of HLFE, or with placebo. After 16 weeks of therapy with 1800 mg of HLFE per day, maximal-tolerated workload during bicycle exercise showed a statistically significant increase in comparison with both placebo and 900 mg of HLFE. Typical heart failure symptoms as rated by the patients were reduced to a greater extent by HLFE than by placebo. This difference was significant for both doses of HLFE. Both efficacy and tolerability were rated best for the 1800 mg of HLFE group by patients and investigators alike. The incidence of adverse events was lowest in the 1800 mg of HLFE group, particularly with respect to dizziness and vertigo.

In the SPICE (Survival and Prognosis: Investigation of Crataegus Extract) study, a randomized, placebo-controlled, double-blind, international trial (approximately 120 investigational centers in seven European countries), up to 2300 patients with congestive heart failure, New York Heart Association class II and III and markedly impaired left ventricular function, will be enrolled and treated over a period of 24 months. During this time, patients will receive either 900 mg HLFE standardized to 170 mg of oligomeric procyanidins or matched placebo per day, in addition to standard therapy for congestive heart failure, such as diuretics, digoxin or digitoxin, β-adrenoceptor blockers, and angiotensin-converting-enzyme inhibitors. The primary outcome variable is the combined endpoint of cardiac death, non-lethal myocardial infarction, and hospitalisation due to progression of heart failure. Secondary outcome variables are mortality, exercise duration, echocardiographic parameters, quality of life, as well as pharmacoeconomic parameters. To date, the results of this trial have not been published.

An interesting clinical study with a novel design was published in 2004. This study compared two different therapeutic strategies in the treatment of NYHA II patients: conventional therapy and HLFE in addition to conventional drugs. In contrast to a standard clinical trial, this was a cohort study where patients were expressly not randomized and the physician in charge independently chose the treatment. In all, 952 patients were enrolled in the study, 588 received Hawthorne extract either as an add-on therapy or on its own (Group 1), and 364 patients received therapy that did not include Hawthorne (Group 2). Only comparable patients in each group were included in the assessment using the matched-pairs technique. After two years, 130 patient pairs were generated and assessed. The results demonstrated that, after two years of treatment, the three cardinal symptoms of heart failure — fatigue (p=0.036), dyspnea on exertion (p=0.020) and palpitations (p=0.048) — were significantly less marked in Group...
Phytotherapy for the Heart

1 versus Group 2. The patients in Group 1 also received significantly fewer conventional drugs than those in Group 2 (ACE inhibitors: 36 vs 54%, p=0.004; cardiac glycosides: 18 vs 37%, p=0.001; diuretics: 49 vs 61%, p=0.061; beta-blockers: 22 vs 33%, p=0.052). The significant aspect of this study was that, not only were there no adverse interactions from combining Hawthorne with these medications, a substantial benefit occurred.

On that specific issue of the interaction of Hawthorne with conventional drugs, HLFE at 900 mg per day had no impact on the pharmacokinetic profile of digoxin in a three-week study. Finally, a recent pilot study assessed the value of Hawthorne with or without magnesium in patients with mild hypertension (n=36) under placebo-controlled, double-blind conditions. Doses were 500 mg/day of HLFE and/or 600 mg/day elemental Mg (an amino acid chelate) for ten weeks. Despite a pronounced placebo effect, non-significant trends for Hawthorne in reducing the number of conventional drugs, HLFE at 900 mg per day had no impact on the placebo effect.

Helicobacter: A Hidden Factor in Cardiovascular, Digestive, Autoimmune, and Skin Disorders

Around 20 years ago, a link between bacterial infection and duodenal and stomach ulcers (peptic ulcers) was suggested. The spiral or helical bacterium known as Helicobacter pylori was first cultured from the stomachs of patients with ulcers in 1982 and is now recognized as the most significant cause of ulcers and gastric cancer. In industrialized countries, the incidence of infection with Helicobacter increases with age, but only a few percent of infected people develop ulcers or cancer. Several reliable diagnostic tests exist for detecting the presence of Helicobacter, and anyone with peptic ulcers or gastric cancer who tests positive is treated with antibiotics for one to two weeks. Usually three antibiotics are given at once (triple therapy) or two antibiotics plus an antacid drug. The success rate for eradication varies between 60 and 90%, depending on the study.

But the story does not just stop here! The majority of people who test positive for Helicobacter do not have peptic ulcers or gastric cancer, but are they free of any adverse effects due to this organism? The answer in many cases appears to be no. In particular, infection with Helicobacter can lead to a condition linked to low gastric acid output known as atrophic gastritis. In fact, the interesting suggestion proposes that much of the reduction in gastric acid output linked to aging is not a natural decline, but is caused by Helicobacter-induced atrophic gastritis.

The implications of this are far-reaching. First, insufficient gastric acid can cause digestive problems such as pain, indigestion, abdominal swelling or bloating, nausea, and vomiting. Low gastric acid can also lead to microbial contamination of the small intestine and even intestinal parasites, since gastric acid is the first line of defense against these organisms. Finally, low gastric acid and damage to the cells lining the stomach can lead to nutrient malabsorption, particularly vitamin B12, iron, and other vitamins and minerals. Studies have shown that eradicating Helicobacter can lead to resolution of atrophic gastritis in many cases.

The effects of Helicobacter infection, however, can reach beyond the digestive tract. In some cases, its presence appears to upset the normal functioning of the immune system, leading to chronic skin disorders and even autoimmune diseases. For example, idiopathic thrombocytopenic purpura (ITP) is an autoimmune disease of unknown origin characterized by a low platelet count and a resultant tendency for the blood to leak from fine blood vessels. An investigation of 16 patients with ITP found that Helicobacter was present in 87%. Eradication of Helicobacter (which was only successful in 64% of cases) led to a complete remission of ITP in more than half of these patients.

Rosacea is a chronic facial skin disease that usually develops at around age 30 to 50 years. It is a chronic condition that can be difficult to resolve. Rosacea has often been linked to poor digestive function, and an association between Helicobacter eradication and improvement of rosacea is now tentatively suggested even in conservative medical circles. In many cases, the eradication of Helicobacter has resulted in complete resolution of this stubborn skin disorder.

A strong link between Helicobacter and chronic urticaria (an allergic skin condition) also exists. For example, eradication of Helicobacter resulted in clinical improvement in 73% of patients with chronic urticaria. Other chronic skin diseases have been implicated. In fact, treatment against Helicobacter should be considered for anyone with a chronic skin or autoimmune disease who tests positive for this organism.

Given the theme of this month's edition of the Townsend Letter, a particular focus will be given here to the suspected but controversial role of Helicobacter in the development of cardiovascular disease. Only about half of coronary artery disease can be explained by the usual risk factors. This has lead to some authorities proposing that infection may be important in the development of atherosclerosis.

A recent study has shown that C-reactive protein, which is a marker of inflammation, is a better predictor of first cardiovascular events than LDL cholesterol. Infection may precipitate or contribute to cardiovascular disease by a variety of mechanisms, including accelerating plaque progression and increasing coagulation.

The strongest evidence for an association between infectious agents and cardiovascular disease is for Chlamydia pneumoniae. However, a role for Helicobacter pylori is only beginning to emerge. A virulent strain of this microbe was associated with coronary disease in Scotland. A recent study suggested that inflammation following H. pylori infection contributes to the early stage of the development of atherosclerosis in younger men. The presence of H. pylori has been associated with nearly double the risk of developing heart disease. A recent review examined the evidence for and against the role of H. pylori in cardiovascular disease. This remains a controversial area which is the focus of ongoing research.

Herbs Active Against Helicobacter

Several herbs have been shown to be active against Helicobacter. Their use is most appropriate when conventional
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