Evaluation of Nutritional Support with Bonito Peptides in Patients with Hypertension: Summary of Clinical Experience

Introduction

Hypertension (HTN) is a serious condition in which increased blood flow exerts undue pressure and stress against the walls of the blood vessels. Nearly 1 in 3 American adults (65 million) have high blood pressure (BP), or HTN. An estimated 30% of them don’t even know it, hence its reputation as “the silent killer.” As the most common primary diagnosis in the U.S., the estimated 2005 direct and indirect cost of HTN is $59.7 billion. HTN forces the heart and blood vessels to work harder than normal, making them highly susceptible to injury. Many studies demonstrate a direct relationship between uncontrolled HTN and increased risk of stroke, heart attack, heart failure, kidney failure, eye problems, and cognitive decline.

Although medications can be effective for some individuals, they may not be the sole approach for addressing HTN. In fact, it has been estimated that only 34% of individuals with HTN respond favorably to drug treatment. While pharmaceutical agents that inhibit angiotension-converting enzyme (ACE) activity have been shown to be relatively safe and to lower BP, they can be accompanied by numerous side effects, including dry cough, dizziness, lightheadedness, headaches, and impotence. In fact, a 2003 survey found that 97% of patients taking antihypertensive medications had suffered from significant side effects at some time. Another survey revealed that nearly 4 out of 10 patients (38%) may stop taking their medications due to drug tolerability problems. Understandably, hypertensive individuals are turning to alternatives known to impact BP favorably.

A Natural Alternative: Bonito Peptides

Commonly prescribed HTN drugs include ACE inhibitors. ACE catalyzes the formation of angiotension II, a potent compound responsible for blood vessel constriction, which in excess, can lead to detrimental effects such as local arterial damage, endothelial dysfunction, blood clot formation, and increased oxidative stress. Due to its physiological effects, angiotension II may be implicated in the pathophysiology of HTN, congestive heart failure, diabetic nephropathy, and in vascular diseases such as atherosclerosis.

Japanese researchers have identified a patented process to isolate specific, active peptides from the bonito fish (Sarda orientalis) with demonstrated blood pressure-lowering effects in animal and human models. The 9 identified, specific active peptides in dried bonito fish include a pentapeptide (LKPNM) that on its own only slightly inhibits ACE. When ACE interacts with LKPNM, however, the pentapeptide is converted into a tripeptide (LKP) that has powerful inhibitory effects against ACE. In fact, the IC50 activity—a measure of the peptide concentration required to inhibit 50% of ACE—of the bonito isolate mixture is approximately 33 µg/mL, which makes it a relatively strong, natural ACE inhibitor.

Bonito peptides provide safe and natural BP support for individuals with pre-HTN (systolic BP: 120-139 mm Hg; diastolic BP: 80-89 mm Hg) or Stage I HTN (systolic BP: 140-159 mm Hg; diastolic BP: 90-99 mm Hg).

Published Research

Clinical Studies

Three human clinical trials have been reported using bonito peptides in subjects with borderline or mild HTN, and have shown significant decreases in BP. In the most recent study, researchers used an optimized bonito peptide mixture of 1.5 grams daily. The results of these case studies suggest that bonito peptides are approximately 64% effective in reducing BP in borderline and mildly hypertensive subjects. In these short-term clinical trials, no serious adverse effects were reported, suggesting that bonito peptides have an excellent safety profile. In an unpublished, pre-clinical pilot study, bonito peptides did not lower BP in subjects with BP already in the normal range. Furthermore, no rebound effect or abnormally high BP levels were observed after supplement termination in short-term trials with borderline and mildly hypertensive subjects.

Figure 1. Data from a study of 30 subjects given bonito peptides have revealed significant decreases in BP, with an average decrease of 11.7 mm Hg in systolic BP and 6.9 mm Hg in diastolic BP after 5 weeks of use.

Case Studies Conducted at the Functional Medicine Research CenterSM (FMRC)

Utilizing the bonito peptides derived from this patented extraction process, we confirmed the findings of third-party clinical research through our in-house case management studies conducted with individuals presenting with Stage I HTN.

Case Study #1

A 55-year-old female presented with HTN, which started at age 25 when she was smoking and considerably overweight (weight: 250 lb). She was initially prescribed an antihypertensive drug and was placed on a second antihypertensive agent at age 35. One year prior to presentation, she hurt her back and was prescribed rofecoxib. Her BP increased and she was placed on a third antihypertensive drug. She quit smoking at age 35 and lost 80 lb with a diet and exercise program by age 45; however, her BP had not improved. She lost an additional 30 lb a year prior to presentation by increasing her exercise activity and had tried an herbal approach for HTN over the previous 2½ months, but her BP remained elevated.
The patient was advised to discontinue the herbal supplement and begin the bonito peptide supplement (500 mg tid), along with a CoQ10 supplement (100 mg bid), and continue her exercise regimen and daily log of BP readings. Over the course of 8 weeks, the patient’s BP reading decreased to 112/70.

**Decrease in Blood Pressure Readings**

<table>
<thead>
<tr>
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<th>Before Program</th>
<th>After 8 Weeks</th>
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<tbody>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>140</td>
<td>112</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>78</td>
<td>70</td>
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Table 1. After 8 weeks, the patient’s BP reading had decreased from 140/78 to 112/70, suggesting considerable improvement.

**Case Study #2**

A 47-year-old overweight Caucasian female presented with HTN that had been diagnosed approximately 2 months earlier with a reading of 144/98 at her naturopath’s office, and she was not on any medication. She was intolerant to gluten and tried to avoid it, and was on a standard American diet with no exercise. Other conditions at presentation included migraines during the second half of her menstrual cycle, PMS, and joint pain that prevented exercise. She had a family history of HTN, diabetes, obesity, stroke, and other heart problems.

Her current medications and supplements included sumatriptan succinate 25 mg prn, L-glutamine prn, L-tyrosine, B complex, DHEA, multiple vitamin, EPA oil, pantothenic acid, thyroid formula, digestive enzymes, calcium, acidophilus, vitamin C, and niacin.

She was advised to start the bonito peptide supplement (500 mg bid), along with a CoQ10 supplement (100 mg bid), continue with dietary (low carb) and exercise recommendations from her naturopath, and monitor her BP morning and evening. Over the course of 12 weeks, the patient showed improvement in BP readings and migraines.

**Average Decrease in Blood Pressure Readings**

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<tr>
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<th>Before Program</th>
<th>After 12 Weeks</th>
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<tbody>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>133</td>
<td>124</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>77</td>
<td>68</td>
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Table 2. After 12 weeks, the patient’s BP readings had decreased from an average of 133/77 to an average of 124/68.

**Case Study #3**

A 53-year-old overweight Caucasian female presented with a history of HTN and obesity. Although she was obese as a child, it was not until her college years that she started experimenting with various weight loss programs, losing and regaining 50-100 lb. She characterized herself as a “stress eater” and found exercising difficult. In her mid-20s, she was diagnosed with HTN, which was inconsistently controlled. She had a family history of HTN, heart disease, and obesity. Her assessment at presentation also included metabolic syndrome and impaired glucose tolerance.

Her medications and supplements at presentation included: lisinopril 10 mg qd, loratadine prn, ibuprofen prn, baby aspirin; multiple nutraceuticals including CoQ10, dehydroepiandrosterone (DHEA), pregnenolone, red rice yeast, guggul, selenium, magnesium, calcium, multiple vitamin, vitamins E and C, vitamin B blend, eicosapentaenoic acid (EPA), gamma-linolenic acid (GLA), and gamma-aminobutyric acid (GABA).

She was instructed to start encapsulated bonito peptides for BP support, 500 mg tid; start a plant sterol and soy protein medical food beverage, 2 servings/day; begin chromium, green tea, cinnamon and alpha-lipoic acid combination supplement for glucose and insulin metabolism support, 2 tablets bid; begin low-glycemic-load diet with no caloric restrictions; increase aerobic activity, working up to 150 min/week; discontinue guggul, vitamin B blend, red rice yeast, vitamins C and E, GLA, magnesium, and calcium; and continue prescriptive medications and other supplements. After 7 weeks, her BP reading had improved to 138/84.

**Conclusion**

The results of these clinical observations suggest that a targeted nutritional support program incorporating bonito peptides daily may help to improve blood pressure in borderline and mildly hypertensive patients.

**References**

11. Case Study: A Case Study Evaluating the Effects of Bonito Peptides and Coenzyme Q10 (CoQ10) in a Patient with Hypertension. Metagenics, Inc; 051HTN804.
12. Case Study: A Case Study Evaluating the Effects of Bonito Peptides and Coenzyme Q10 (CoQ10) in a Patient with Hypertension. Metagenics, Inc; CS00287.
14. Case Study: A Case Study Evaluating the Effects of Bonito Peptides and Coenzyme Q10 (CoQ10) in a Patient with Hypertension. Metagenics, Inc; CS00287.
16. Case Study: A Case Study Evaluating the Effects of Bonito Peptides and Coenzyme Q10 (CoQ10) in a Patient with Hypertension. Metagenics, Inc; CS00287.
18. Case Study: A Case Study Evaluating the Effects of Bonito Peptides and Coenzyme Q10 (CoQ10) in a Patient with Hypertension. Metagenics, Inc; 058HTN804.

Note

Case Studies Conducted at the FMRC

The information provided in each of these case studies describes the results of one patient under the care of a licensed healthcare practitioner and may not be a typical response. The case studies were conducted at the Functional Medicine Research Center (FMRC), the clinical research arm of Metagenics, Inc. Robert Lerman, MD, is the Medical Director of the FMRC. Financial support was provided by Metagenics, Inc.

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