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# 'Medical Food' Bests Ibuprofen in Chronic Low Back Pain

Pauline Anderson | October 07, 2014

Theramine, a "medical food" containing an amino acid blend (AAB), significantly improves chronic low back pain and reduces inflammation compared with low-dose ibuprofen, a nonsteroidal anti-inflammatory drug (NSAID), or a combination of these 2 treatments, results of a new study show.

This is the second study looking at theramine in low back pain. The first (*Am J Ther*. 2012;19:108-114) compared this medical food with another NSAID, naproxen.

"Now we have done 2 multicenter, double-blind trials showing the effectiveness of theramine, not only on pain but also inflammation, and we are not seeing significant side effects," commented study author David S. Silver, MD, president and chief operating officer, Targeted Medical Pharma Inc, Los Angeles, California.

Observers have expressed both encouragement and reservation about this study, which was published online September 18 in the *American Journal of Therapeutics*.

**Dietary Amino Acids**

Back pain affects up to 90% of people during their lifetime. Chronic low back pain is the number one cause of time lost from work, said Dr Silver.

NSAIDs are frequently prescribed to treat chronic back pain, and among these, ibuprofen is the most commonly prescribed.

It's believed that patients with chronic pain have decreased levels of neurotransmitters responsible for pain inhibition and control of inflammation, the authors note. There's evidence in plasma of a deficiency of amino acid precursors that are important to chronic pain modulation, said Dr Silver, a rheumatologist who has treated patients with fibromyalgia in his Los Angeles, California, practice.

It's not possible to treat pain by boosting amino acids through the diet, Dr Silver said. "You can't just take amino acids and hope that you're going to produce neurotransmitters" to control pain, he said. Dietary amino acids may not be adequately absorbed, may be deaminated by the liver before crossing the blood-brain barrier, and may not be taken up by the appropriate neurons, he noted.

Current pain therapies don't adequately address these issues, said Dr Silver. NSAIDs, for example, are only moderately effective in relieving pain and are associated with significant gastrointestinal adverse effects. Other pain treatments, including muscle relaxants and opioid analgesics, have limited efficacy, may produce sedation and constipation, can be used inappropriately, or can lead to addiction issues.

"We think theramine fits very nicely into that void," said Dr Silver.

As a "medical food," theramine does not require US Food and Drug Administration preapproval; however, everything in the product must be GRAS (generally recognized as safe), said Dr Silver. "The claims [of a medical food] must be specifically for the nutritional management of a disease when a distinct nutritional

requirement that cannot be met through regular diet is recognized," he said.

The claims of medical foods must be supported by clinical studies, unlike dietary supplements or nutraceuticals, which can't make disease claims and don't require clinical studies, he added.

Through its cellular technology, theramine is designed to specifically target precursors to neurotransmitters involved in pain and inflammation (acetylcholine, histamine, serotonin, D-serine, and nitric oxide).

**Multicenter Study**

The new eight-site, three-arm study was funded by Targeted Medical Pharma. It included 122 patients aged 18 to 75 years who had back pain lasting longer than 6 weeks, with pain present on 10 of 14 days, and evidence of at least moderate pain.

The individual study sites were entirely responsible for recruiting study participants, said Dr Silver. Patients were not paid to participate in the study and were reimbursed only for reasonable expenses, such as travel costs.

The patients were randomly assigned to one of three groups: two AAB tablets twice a day with one ibuprofen placebo; ibuprofen (400 mg once daily) with two AAB placebos twice a day; or two AAB tablets twice daily with ibuprofen (400 mg once a day).

The researchers used the lowest recommended dose of ibuprofen because, explained Dr Silver, "we didn't feel that utilizing placebo for patients with chronic pain was ethical, and we didn't want to expose patients to a higher risk of NSAID-induced complications by using high-dose therapy."

After 28 days, participants were evaluated by using the Roland-Morris Disability Index and the Oswestry Disability Scale (primary endpoints), as well as a visual analogue scale (VAS).

**Significant Improvement**

The study showed that in both the AAB and combined therapy groups, pain assessments were considerably and statistically significantly improved compared with the ibuprofen-alone group. In the AAB-alone group, the Roland-Morris Disability Index score fell by 50.3% and the Oswestry Disability Scale score fell by 41.91% ($P < .05$ for both vs ibuprofen).

In the combination group, the Roland-Morris Index fell by 63.1% and the Oswestry Disability Scale score fell by 62.15% ($P < .05$ for both vs ibuprofen). Similar results were observed with use of the VAS.

The study also showed improvements in measurements of inflammation in patients taking AAB. From blood samples, researchers found that in the AAB-alone group, the C-reactive protein (CRP) level fell by 47.05% and the interleukin-6 (IL-6) level fell by 23.55% ($P < .001$ for both vs ibuprofen). In the combined group, CRP fell by 35.99% and IL-6 fell by 43.1% ($P < .001$ for both).

Interestingly, in the ibuprofen alone group, levels of CRP rose by 60.1% and IL-6 rose by 12.65%.

Dr Silver noted that the previous head-to-head study of theramine and naproxen also showed a reduction in inflammatory markers in persons taking the medical food. "So not only is it a pain-relieving agent, but it does seem to reduce inflammation."

Since CRP indicates inflammation, which may be involved in heart disease, theramine could also have cardioprotective qualities, said Dr Silver, although he stressed that this has not been studied.

It's not clear why inflammatory markers increased in patients taking ibuprofen in this study, said Dr Silver. Again, this was the second time that his research group has shown this effect. It could be because NSAIDs are antiprostaglandin drugs and not necessarily anti-inflammatory drugs, he said.

He added that rheumatologists don't rely on NSAIDs "as our big anti-inflammatory agents," but rather on other medicines, such as methotrexate, an antifolate drug used to treat some autoimmune diseases, such as rheumatoid arthritis.

None of the patients taking theramine in this new study experienced any significant adverse effects, said Dr Silver. No gastrointestinal adverse effects were observed or reported.

The overall results suggest that theramine can be used as a primary therapy or an adjunct to ibuprofen, said the authors.

Although a dose of two AAB capsules twice daily was used in the study, Dr Silver has used up to eight a day to treat some patients. However, he doesn't think there would be any benefit beyond that. "At some point, you're going to get a threshold effect," he said.

**Other Populations**

Dr Silver is investigating the effectiveness of theramine in other patients with pain. He and his colleagues are studying this product in chronic migraine and are finalizing a plan to study it in military personnel with back pain. Another study will investigate theramine in patients who have had a hemorrhoidectomy, in whom narcotics are contraindicated because of constipation issues.

Theramine is available in pharmacies but since it's classified as a medical food, it must be used under medical supervision, said Dr Silver.

When approached for a comment, Lynn Webster, immediate past president, American Academy of Pain Medicine (AAPM) and vice president, scientific affairs, PRA Health Science, said he was heartened by the study.

"We ought to be encouraged about research in areas that can provide us with any type of medication that is safer," he told *Medscape Medical News*. "It appears that this whole new class offers hope that we will be able to have fairly effective therapies for some conditions, particularly for pain, that are safer than what we have now."

Also asked to comment, Christopher Standaert, MD, professor, Rehabilitation Medicine, University of Washington, Seattle, said he couldn't provide "a formal comment" because he felt he didn't know enough about the relevant pharmacology and serum chemistry to determine the validity of the study from that perspective.

However, he did raise some issues "to think about." These included the following:

1. The study was of a commercial product. It was apparently performed by the company that makes that product and conducted at commercial sites funded by the same manufacturer.

2. The paper doesn't include the raw data on outcomes — only percentages of improvement — and doesn't discuss issues such as the success of blinding and patient adherence.

3. There is little information on the study patients and how they were recruited.

4. Although the authors discuss the negative aspects of NSAIDs, they don't say much about potential downsides of the drug under study.

*The study was funded by Targeted Medical Pharma, maker of theramine. Dr Silver is president of the company. Dr Standaert has disclosed no relevant financial relationships.*

*Am J Ther*. Published online September 18, 2014. Abstract



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Cite this article: 'Medical Food' Bests Ibuprofen in Chronic Low Back Pain. *Medscape*. Oct 07, 2014.