Nutrition and Pain Management: Putting Pain Relief on the Menu

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In This Issue

Nutrition and Pain Management: Putting Pain Relief on the Menu.............99
How Research Translates to Supplement Innovation..................................106
Potential Botanical Use in Pain Management............................................108
News You Can Use......................................................................................111
Mind and Body Practices for Pain Management: The Pilates Method and Chronic Low Back Pain..........................................................116
Hyperuricemia and Related Painful Diseases..........................................120
A Nutritional Approach to Cognitive Decline..........................................124
Chair’s Corner..............................................................................................128
Editor’s Notes..............................................................................................129
Executive Committee List............................................................................130

Nutrition and Pain Management: Putting Pain Relief on the Menu

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ith the current opioid epidemic, nonpharmacologic pain management is receiving unprecedented attention. In a widely reported clinical practice guideline, the American College of Physicians recommends trials of evidence-based nonpharmacologic modalities—acupuncture, exercise, cognitive behavioral therapies—before pharmacologic treatments for chronic pain.1,2 Dietary interventions are noticeably absent from this list of evidence-based approaches to pain management.

Is there no evidence base for nutrition in pain management? To the contrary—evidence exists, but the connection between food and pain is multifactorial, and cause and effect is not always linear. This article will review evidence in four distinct areas of the relationship between nutrition and pain: nutrient insufficiencies, inflammatory load, the potential role of the microbiome, and overall eating patterns.

Before describing such mechanisms, let us look at why nutrition may not currently be on the short list of nonpharmacologic pain management interventions.

Nutritional therapy for pain has been used in nonwestern systems of healing, such as Chinese Medicine and Ayurveda, for thousands of years. In modern pain management, we think of pain diagnosis in terms of identifying pain generators, such as an arthritic hip, a damaged nerve, or a sprained muscle. We seek ways to repair structural damage, block discrete receptors, or inhibit specific pathways. A nutritional approach to pain is fundamentally different. Instead of isolating one cause and correcting the corresponding culprit, the nutritional approach is global, in support of the whole organism’s innate ability to heal, and often works preventively.

There are economic factors that influence the lack of awareness of the benefits of nutrition for pain management. The financial return on investment for studying nutritional remedies for pain is low. An anti-inflammatory diet cannot be patented, and well-designed nutritional studies can be lengthy, laborious, and do not lead to the development of a new product. In addition, nutrition professionals are not always included as key participants in pain management circles.

CPE Objectives:
After reading this article, the nutrition professional will be able to:
1. Discuss three mechanisms that explain the relationship between nutrition and pain.
2. Describe the basic components of an anti-inflammatory diet and the contribution of each component to balancing inflammation levels in the body.
3. List three chronic pain conditions which have been shown to be directly related to nutrient insufficiencies.
4. Recognize the potential role of the microbiome in modulation of inflammation and pain.

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Introduction and Context

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members of the medical team. However, understanding the science and using current evidence to support greater awareness and advocacy will help put nutrition on the map for treatment of chronic pain.

**Nutrient Insufficiencies**

If we look for a nutrient insufficiency model to link pain and nutrition, there are a few micronutrients that stand out.

**Magnesium**

Magnesium is necessary for over 300 physiologic reactions, and magnesium deficiency is estimated to be widespread and rising in the US and Canada. Magnesium deficiency is associated with migraine headaches, and repletion is associated with prevention of headaches as well as treatment of acute migraine. Magnesium administration has been associated with relief of premenstrual syndrome (PMS) and fibromyalgia. Recommended oral dosages are 400-600 mg per day.

**Vitamin C**

Vitamin C is important for bone healing and collagen crosslinking, as well as its role as an antioxidant.

In order to investigate whether vitamin C may prevent the development of complex regional pain syndrome (CRPS), Zollinger et al followed a group of 317 patients with wrist fractures who were randomized to receive either 200, 500, or 1500 mg of vitamin C and 99 patients who were randomized to receive a placebo. The prevalence of CRPS was 2.4% in the vitamin C group and 10.1% in the placebo group; all the affected patients were elderly women who may have been nutrient deficient. The prevalence of CRPS was 4.2%, 1.8%, and 1.7% in the 200, 500, and 1500 mg groups respectively. The optimal dosage of 500 mg has been confirmed by subsequent studies.

A group of Canadian researchers examined the associations between serum vitamin C concentration and the prevalence of spinal pain and functional limitations in over 4000 adults in the general US population using data from the 2003-2004 US National Health and Nutrition Examination Survey (NHANES). Suboptimal serum vitamin C concentrations were associated with the prevalence of neck pain and low back pain in the previous three months and related functional limitation score.

Vitamin C decreases the requirement for opioid analgesics, especially post surgically, and may be effective for cancer pain and for pain associated with chronic pancreatitis.

**Other Nutrients of Concern**

Good evidence exists for the use of intravenous alpha lipoic acid for diabetic neuropathy, and some studies show a benefit of an oral dose of 600 mg with and without vitamin B12.

Preliminary evidence exists for a preventative effect of vitamin D and B vitamins on pain of various etiologies, but there is not enough evidence to make clinical recommendations at this time.

Nutrient groups such as phytonutrients and essential fatty acids are best discussed within the context of dietary eating patterns (below).

**Pain and Inflammatory Load**

Nearly all pain has a component of inflammation.

This can be profoundly influenced by diet. A pro-inflammatory diet, such as the Standard American Diet (SAD), contains several elements that promote systemic inflammation; and there are a number of diets that are considered anti-inflammatory. Below is a table comparing the dietary components that determine the degree of inflammation contributed by diet.

<table>
<thead>
<tr>
<th>Pro-inflammatory Diet</th>
<th>Anti-inflammatory Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low in phytonutrients</td>
<td>High in phytonutrients/spices</td>
</tr>
<tr>
<td>Low fiber</td>
<td>High fiber</td>
</tr>
<tr>
<td>High glycemic load</td>
<td>Low glycemic load</td>
</tr>
<tr>
<td>High in animal protein</td>
<td>Low to moderate animal protein</td>
</tr>
<tr>
<td>Highly processed</td>
<td>Basic preparation</td>
</tr>
</tbody>
</table>

**Fat balance**

Dietary fat is one of the most important determinants of the inflammatory load. The content of dietary fat will determine the essential fatty acid (EFA) balance that is metabolized by the EFA pathway. The essential fats linoleic acid (LA) and alpha linolenic acid (ALA) are called essential because they are not manufactured in the body and must come from the diet.

The pro-inflammatory omega-6 pathway begins with LA and produces arachidonic acid, the precursor to pro-inflammatory cytokines, prostaglandins, thromboxane, and leukotrienes. Prostaglandins sensitize peripheral nociceptors (pain receptors), while leukotrienes increase vascular permeability. The cytokines produced by the pro-inflammatory pathway are responsible for multiple aspects of the inflammatory process, including the initiation and persistence of pain. These proteins can sensitize nociceptive neurons, contribute to central sensitization, and influence the development of hyperalgesia and allodynia.

The anti-inflammatory omega-3 (ω-3) pathway begins with ALA and produces eicosapentaenoic acid and...
Antioxidant Phytonutrients

Chronic inflammation produces free radicals, which can deplete stores of antioxidants and lead to a state of oxidative stress, or “inflammaging.” Certain nutrients, such as magnesium and zinc, are cofactors in key enzymatic reactions that dismantle free radicals. Others, such as vitamin C and phytonutrients, are dietary antioxidants that quench oxidation. When cofactors and coenzymes are deficient, oxidation increases.21

We know that fruits and vegetables, herbs and spices, and green tea contain bioactive compounds such as flavonoids, carotenoids, and proanthocyanidins. These compounds reduce the oxidative stress that results from chronic inflammation. There is evidence that soy foods may contribute to pain reduction.23 Data from the British Cohort study, which follows children from birth, revealed an association between a decreased intake of fruits and vegetables and chronic widespread pain.24 Pain scores of patients with knee pain decreased significantly with increased intake of fruits and vegetables,25 and patients with osteoarthritis experienced decreased pain with a whole foods, plant-based diet.26 Fibromyalgia has been shown to be responsive to vegetarian diets,27,28 and a higher consumption of fruits and vegetables has a protective effect for gout.29 Isolated phytonutrients have been associated with decreased postsurgical pain,30 reduced lower extremity pain,31 and less exercise-induced muscle soreness.32 There is a robust literature devoted to the anti-inflammatory properties of green and black tea as well as many herbs, covered later in this issue.

Fiber and Glycemic Load

Carbohydrate foods influence the inflammatory process. There is a correlation between postprandial glucose concentration, oxidant stress, and inflammation.33 Fiber in the diet slows absorption time of sugars and helps to optimize glucose metabolism, which avoids a high glycemic load and an insulin-driven rise in C-reactive protein (CRP).34,35 Some types of fiber act as prebiotics and support growth of symbionts (helpful bacteria) in the intestine, promoting a diverse microbiome and balanced immune response. The degree of “westernization” of a diet is associated with a decrease in microbial diversity, which includes organisms that process fiber-rich dietary components.36 Reviews of the data of two prospective studies—the Osteoarthritis Initiative and the Framingham Offspring Osteoarthritis Study—show that dietary fiber was significantly and inversely associated with worsening of knee pain in people with osteoarthritis.37 An analysis of more than 15,000 NHANES participants showed significant associations between systemic inflammation, as indicated by high levels of CRP, and low back pain, especially in those who were obese.38

Protein

Protein from conventionally-raised animals, with a higher content of arachidonic acid than grass-fed animals, may contribute to inflammation.39 Cold-water fish contribute ω-3 fatty acids, which help to modulate the inflammatory response.40 Proteins found in plants, such as legumes and vegetables, are accompanied by phytonutrients.

The Gut Microbiome and Pain Modulation

The term microbiome refers not only to the microbes in a specific environment but also to the environment that they inhabit. The gut microbiome includes the gut epithelium, immune components, and products of both the microbes and host, including metabolites.41 Microbiota refers to the organisms themselves. The gut microbiota is comprised of approximately 100 trillion cells,42 and it has been compared to a separate organ in terms of the complexity of its metabolic activity.43 This metabolic activity is linked to multiple chronic conditions: metabolic syndrome, obesity, and cardiovascular disease.44 Beneficial bacteria act to block pathogen colonization by competing for nutrients and space and by synthesis of bacteriocidal products,45 vitamin production, and modulation of inflammation.

Although there is no linear connection between the microbiome and pain, there are multiple complex relationships to be considered. Gut microbes play an important part in the maintenance of systems that contribute to pain modulation. Microbes in the gut produce B vitamins and vitamin K; the B vitamins especially are important cofactors for methylation and essential fatty acid metabolism, which in turn are part of the landscape of inflammation.46 Gut microbes convert nutrients such as lignans and isoflavones to their usable forms. Among other functions, both contribute to modulation of inflammation.46-48 As we have seen previously, systemic inflammation...
Some beneficial bacteria have immunomodulating effects, which in some cases may depend on the health status of the host: down-regulating immune function in people with immune system hypersensitivity and stimulating it in healthy people. Lastly, the manipulation of some microbial species by use of prebiotic foods may decrease visceral pain.

Beneficial bacteria play an important role in the maintenance of a healthy enterocyte layer in the intestinal tract. The interaction of microbiota with the immune system affects secretory IgA, release of antimicrobial substances, and maintenance of the protective mucosal layer.

An aspect of nutrition and pain management that cannot go unnoticed is food sensitivity and the resulting increased gut permeability as a source of inflammation, autoimmunity, pain, and physical dysfunction. Although an in-depth review is outside of the scope of this article, it is reviewed well elsewhere.

In essence, the gut microbiome interacts with multiple metabolic processes that then have an effect on pain and chronic conditions associated with pain and may be used in support of nutritional pain management approaches.

Examples of Anti-inflammatory Eating Patterns

Three eating patterns from diverse areas of the world—the Mediterranean Diet, the Okinawan Diet, and the diet of the Native Kuna in Panama—all use foods native to the geographic region from which they originate. The Mediterranean Diet utilizes native olives and olive oil, the Okinawan Diet is rich in seafood and sea vegetables, and the Kuna diet contains a great deal of flavanol-rich cacao. At the same time, each illustrates the qualities of plant-based, high fiber, low glycemic diets with high quality protein.

Conclusion

The use of nutrition for pain management is an evidence-based nonpharmacologic intervention that can contribute significantly to a comprehensive approach to chronic pain. Although the evidence base is not complete, there is data that shows relationships at the level of single nutrients as well as dietary patterns.

Our success in establishing dietary intervention as fundamental to pain management depends in part on our ability to guide health care practitioners and patients to recognize its role and to understand the nature of its contribution.

It may be helpful to guide patients and their referring clinicians about the theoretical basis for this approach, as well as the scope, timeline, and potential limitations of using nutrition for pain management. Nutrition should be recommended as part of a long-term strategy for managing chronic pain, instituted gradually while shorter-acting therapies (eg, acupuncture, medication, manual therapies) are used to provide pain relief in the near term. As patients experience pain relief with other modalities, they are more able to make changes in dietary habits.

It is helpful to provide some guidance for patient expectations. With an anti-inflammatory diet, improvement (increased function or decreased need for medication) will often be noticed in 3-6 weeks. For patients who may be reacting to specific foods, partial pain relief may be evident in a shorter time period after such foods are removed. Although dietary change is potent, it is rarely the only tool needed for relief from chronic pain and is best used as part of a multi-modality approach. Often, nutritional therapy potentiates the success of other modalities.

Nutrition intervention for chronic pain care is not yet as widespread as it is for other chronic conditions, such as cardiovascular disease and diabetes. Reasons for this include lack of training on the part of providers, market forces, and time pressure in the office. As we better understand the relationship between dietary patterns, the microbiome, immune modulation, and pain, the contribution of nutrition to pain prevention and treatment will become more evident. By educating both patients and providers about the powerful role nutrition can play, registered dietitian nutritionists can take the lead in bringing dietary interventions to the forefront of chronic pain management.
Figure 1: Essential Fatty Acid Pathway

With permission, courtesy of Adam Rindfleisch, MD, University of Wisconsin Integrative Health, Veterans Health Administration Office of Patient Centered Care and Cultural Transformation
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This activity has been approved for 1.0 hours of CPE credit. You will be notified if hours are not approved.
Suggested Learning Needs Codes: 2070, 2090, 2100 and 5420.
Suggested Performance Indicators: 8.1.3, 10.4.4, and 10.4.5

Questions:

1. Which of the following nutrients has been shown to decrease the requirement for opioid analgesics post-operatively?
   A. Magnesium
   B. Alpha linolenic acid
   C. Vitamin C
   D. Alpha lipoic acid

2. Which of the following was shown to be inversely associated with worsening of knee pain in people with osteoarthritis?
   A. Phytonutrients
   B. Dietary fiber
   C. Protein intake
   D. Glycemic load

3. Pro-inflammatory cytokines are derived from which of the following?
   A. Eicosapentaenoic acid
   B. Alpha linolenic acid
   C. Docosohexaenoic acid
   D. Arachidonic acid

4. The gut microbiota has been compared to a separate organ due to its:
   A. Ability to block pathogen colonization
   B. Complex metabolic activity
   C. Immunomodulating effects
   D. Effect on pain and chronic conditions

5. An anti-inflammatory diet would include which of the following dietary components?
   A. Low glycemic load, high fiber, high in phytonutrients
   B. Low to moderate animal protein, minimal trans fats, low fiber
   C. High omega-6 to omega-3 ratio, high glycemic low, high fiber
   D. Whole/minimally processed foods, high animal protein, low phytonutrients
Putting Pain Relief on the Menu

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