INTEGRATIVE MEDICINE TREATMENT OF OSTEOARTHRITIS: TIME TO THINK OUTSIDE THE JOINT

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Integrative Medicine Approach to Osteoarthritis: Time to think outside the joint

WHAT I’D LIKE TO CONVEY:

- We can think of osteoarthritis as a local manifestation of a systemic process

- If we treat systemically, the local symptoms resolve more easily

- Diet has a substantial impact on inflammatory load

- The tools of an anti-inflammatory diet, anti-inflammatory botanicals, manual therapies and acupuncture are within reach of most physicians to use
Osteoarthritis

- Most prevalent form of arthritis; 27 million currently
- Prevalence expected to increase dramatically over next 20 years
- Second only to ischemic heart disease as a cause of work disability
- Economic burden $12,000/person/yr; $60 billion/yr
  Gupta S, Hawker G A et al Rheumatology 2005 44(12):1531-1537
- 1-2.5% of GDP in industrialized countries
- By age 40, most people have some arthritis in a weight bearing joint
Osteoarthritis: Case Study

- Patricia McCullough, 62 year old caucasian female (Irish/Scottish descent) has had arthritis “for years in my knees- Motrin works partially, but it hurts my stomach”
- Experiences 6-10/10 pain with weight bearing, worse with damp and cold weather and at end of day
- Stairs and vacuuming particularly difficult
- Medical History: hypercholesterolemia; on Lipitor
- Caring for husband, grandchildren, mother, mother in law, working 24 hours per week, and active at church
- Recently told by Orthopedist that next step is total knee replacement- come back when the pain is bad enough
- Will “do anything” to prevent surgery- “I’m too young!”
Osteoarthritis: Case Study

- **Physical exam:**
  - Overall well developed well nourished 62 y.o. Female
  - Height 5’ 4” Weight 168 lb, central weight gain
  - Functional range of motion of C- and L- spine, upper and lower extremities

- **Joint exam:**
  - Knees show osteoarthritic changes, widening of tibial plateau, medial compartment tenderness R> L
  - Right hand has one Heberden’s node 3rd PIP

- Gait is antalgic on right
- Labs: CRP, sed rate, WNL

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what are her options?
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Osteoarthritis: Case Study

- Began PT which included manual therapy, release of tight tissues in the entire lower extremity, strengthening program and at home exercises
- Began a three week elimination diet: eliminated refined foods, wheat, dairy, sugar, caffeine, corn, soy, shellfish, tomatoes, peanuts for three weeks, followed by 3 day test period for each; joint pain, gas and bloating with wheat
- Began to take:
  - Omega three fatty acids 3000 mg DHA + EPA / day
  - glucosamine sulfate 1500 mg daily
  - Anti-inflammatory herbal prescription
  - High – quality probiotic
- Began periosteal acupuncture with electrical stimulation
Osteoarthritis: pathophysiology

Normal Joint function:

- **Synovium**: lining consisting of a few layers of cells within the joint capsule forming barrier for joint; manufactures synovial fluid
- **Cartilage**: lines articular surfaces and provides protection for underlying bone
- **Bone**: supports muscular attachments across joint and remodels in response to loading
- **Synovial fluid**: acts as lubricant and shock absorber; contains hyaluronic acid
Osteoarthritis: pathophysiology

Abnormal Joint function: OA is an inflammatory condition

- Cartilage: breaks down faster than replacement cartilage can be made in response to joint overloading or increased inflammatory load

- Bone: remodels in response to abnormal/excessive loading due to excess weight, weakened muscles, insufficient or decreased nutrition in joint fluid

- Synovial fluid: becomes depleted of sulfated proteoglycans which act as lubricant and shock absorber
Osteoarthritis: pathophysiology

Abnormal Joint function: OA is an inflammatory condition

- Weight bearing in and of itself may cause release of inflammatory mediators in some patients

- Weight gain produces increased inflammatory cytokines, therefore, loss of fat produces not only less weight on the joint, but decreased IL-1

- Synovium: lining becomes inflamed and manufactures synovial fluid with decreased concentration of normal hyaluronic acid
Osteoarthritis: pathophysiology

- Primary Osteoarthritis: “wear and tear” cartilage destruction and joint deformity occurring in 5th decade and beyond with no predisposing factors.

- Secondary Osteoarthritis: predisposing factors such as trauma, congenital malformation, previous inflammatory disease of the cartilage/joint (ie RA, septic arthritis), crystal deposition.

- Weight bearing joints and peripheral and axial joints preferentially affected.

- Deformations commonly seen include widening of the tibial plateau, Heberden’s nodes (proximal interphalangeal joints-common) Bouchard’s nodes (distal interphalangeal joints).
Assessment of Osteoarthritis: symptoms

- Morning stiffness
- Joint swelling
- Pain on weight bearing, relief at rest and with heat
- Knees: initial pain is usually medial compartment
- Hips: “deep” pain sometimes radiating anteriorly
- Hands: swelling of fingers
Assessment of Osteoarthritis: signs

- Weight bearing joints and peripheral and axial joints preferentially affected
- Joint swelling
- Hands: swelling of fingers, Heberden’s and Bouchard’s nodes
Assessment of Osteoarthritis: signs

- **Knees**: widening of the tibial plateau, osteophytes, deformation of knee joint; may affect range of motion
- **Hips**: ROM affected; internal rotation is first part of range to be affected
Assessment of Osteoarthritis: Laboratory Evaluation

- Radiographic studies (necessary)
- Vitamin D levels (important)
- Assess Inflammatory load (when appropriate)
  - C-reactive protein (CRP)
  - Erythrocyte sedimentation rate (ESR)
  - Essential Fatty Acid (EFA) levels
  - Gut ecology
- Assess potential for food allergies (food antibody profile or elimination diet)
Assessing Osteoarthritis: Laboratory Evaluation

Radiographic studies

- Joint deformity
- Irregular joint surface
- Loss of joint space
Assessing Osteoarthritis: Laboratory Evaluation

- Vitamin D levels
  - Vitamin D deficiency and musculoskeletal pain
  - Vitamin D deficiency associated with OA, osteoporosis, inflammatory conditions
    Holick, Michael F. MD, PHD Southern Medical Journal. 2005;98(10):1024-1026,
Assessing Osteoarthritis: Laboratory Evaluation

For patients with background of other inflammatory processes:

- Assess level of systemic inflammation
  - C-reactive protein (CRP)
  - Erythrocyte sedimentation rate (ESR)
  - Essential Fatty Acid (EFA) levels: indicate ratios of \( \Omega6:\Omega3 \) fatty acids which influence level of systemic inflammation and indicate degree of replacement needed
Assessing Osteoarthritis: Laboratory Evaluation

- Assess potential for food allergies (food antibody profile or elimination diet)
  - High percentage of gluten sensitivity in Europeans
  - Gluten sensitivity may contribute to joint inflammation
  - Elimination diet may be better indicator than food allergy profile
  - May need to further assess digestive function

Assessing Osteoarthritis: Dietary considerations: Standard American Diet (SAD)

SAD is a pro-inflammatory diet

- Simple sugars
- Relatively high in meat and fat from grain-fed animals
- Fried foods and trans fats
- Non-foods/recreational foods
- Lower proportion of fruits and vegetables in diet
- Higher in Omega-6 fatty acids
Pain and the anti-inflammatory approach

- Inflammatory mediators are also pain mediators: IL2, MCF, TNF, therefore……
- Decreasing inflammatory load decreases pain

Anti-inflammatory Diet and Supplements:
- Eliminate foods that are pro-inflammatory
- Improve overall nutritional status: increase tissue responsiveness to natural supplements or anti-inflammatory pharmaceuticals

Exercise and weight loss:
- Increase lean muscle mass: adipose tissue produces adipokines which likely contribute to joint inflammation separately and distinctly from mechanical stress
Treating Osteoarthritis: Anti-inflammatory Diet

- Avoid *trans* fats and sources of arachidonic acid
- Limit saturated fat
- Emphasize foods with abundant omega-3 content; eat fish 3x/week; adjust omega-6–to–omega-3 ratio
- Eat 5-9 servings of fruits and vegetables/day
- Use antioxidant herbs and spices
- Eat 25 g fiber/day
- Optimize glucose metabolism
Omega 6 Fatty Acid (Linoleic Acid)

Δ6-Desaturase

Gamma-linolenic acid (GLA)
Evening Primrose Oil
Borage Oil/ Black Current Oil

Δ5-Desaturase

Dihomogammalinoleic acid (DGLA)

Elongase

Arachidonic Acid

Cyclooxygenase (COX)

Prostaglandins (PGE1, PGE3)
(less inflammatory)

Leukotrienes

Lipoxygenase

Prostaglandins (PGE2)
(Inflammatory)

Omega 3 Fatty Acids (alpha-linolenenic acid)

Δ6-Desaturase

Eicosatetraenoic acid

Elongase

Eicosapentaenoic Acid (EPA)

Cyclooxygenase (COX)

5-Leukotrienes (less inflammatory)

Docosahexaenoic acid (DHA)

Lipoxygenase (LOX)

Eicosatetraenoic acid

Elongase

Eicosapentaenoic Acid (EPA)

Cyclooxygenase (COX)

5-Leukotrienes (less inflammatory)
Omega-6 fatty acids (linoleic acid)

Gamma-linolenic acid (GLA)

Dihomogamma-linolenic acid (DGLA)

Arachidonic acid (AA)

Cyclooxygenase (COX)

Lipoxygenase (LOX)

Eicosatetraenoic acid

Eicosapentaenoic acid (EPA)

Docosahexaenoic acid (DHA)

Prostaglandins (PGE2) (inflammatory)

Leukotrienes

Prostaglandins (PGE1, PGE3)

5-Leukotrienes

Anti-Inflammatory herbs and spices

Δ6-Desaturase

Elongase

Δ5-Desaturase

Δ4-Desaturase

Trans fats

Omega-3 fatty acids (alpha-linolenenic acid)

Stearidonic acid (SDA)

Δ5-Desaturase

Elongase

Eicosapentaenoic acid (EPA)

Lipoxygenase (LOX)

5-Leukotrienes

Docosahexaenoic acid (DHA)
Omega 3 Fatty Acids

- SAD 10:1 to 25:1 n=6 to n=3 Omega FA
- 4:1 adequate for healthy individuals
- 1:1 preferred in inflammatory conditions for treatment phase
- Fish oils: Mackerel, herring, salmon bluefish tuna, sardines
- Flax seed oil or algae source for vegetarians

Covington M Am Fam Phys 2004 ; 70: 133-40
Recommended intake Omega-3 fats:

- Cardiac prevention 1g EFA/day
- Joint Maintenance 2.5 g/d Strive for Omega 6: Omega-3 ratio of 4:1
- Pain management/treatment chronic pain up to 4.5 g/d

Covington M Am Fam Phys 2004; 70: 133-40
Treating Osteoarthritis: Omega 6: Omega 3 ratio

- Omega-6-rich fat consumption is associated with increased production and responsiveness to pro-inflammatory cytokines.
- Omega-3-rich fats decrease responsiveness to cytokines.


Anti-inflammatory Spices


Anti-inflammatory Spices

Cloves

Cinnamon

Ginger

Garlic
Treating Osteoarthritis: Anti-inflammatory Diet

- Eat 5-9 servings of fruits and vegetables/day
- Eat 25 g fiber/day

Bartali, B et al: Low Micronutrient Levels as a Predictor of Incident Arthritis in Older Women Archives of Internal Medicine 2006166(21):2335-2340
Treating Osteoarthritis: Anti-inflammatory Diet

Optimize glucose metabolism

- Low-insulin response diet may decrease plasma CRP.

- High glycemic load correlates positively with plasma CRP.
Most OA diet studies focus on weight loss, not composition of diet. However, several studies have looked at diet in Rheumatoid Arthritis:


Exercise and Osteoarthritis

- Physical Therapy LE
  - Education
  - Pelvic girdle strengthening
  - Hip range of motion
  - Knee strengthening, especially quads
  - Myofascial release of ITB, quads, hamstrings, gastroc-soleus
  - Bracing, heel wedges, viscoelastic inserts, knee taping

- Occupational Therapy
  - Education on joint conservation
  - Hand conditioning for stiffness and strengthening
  - Postural education for cervical and shoulder OA
Physical Medicine and Osteoarthritis: Exercise and conditioning

Exercise and Osteoarthritis

- **Yoga**
  - Maintains flexibility and balance
  - Lunges evenly build knee strength
  - Regular stretching through range of motion decreases myofascial restrictions on joints
  - Can be designed to maintain PT goals

- **Tai Chi**
  - Gentle ranging of joints
  - Gradually and safely builds strength
  - Maintains balance and prevents falls
Physical Medicine and Osteoarthritis: Acupuncture

- Kwon, Y. D. 1,2; Pittler, M. H. 1; Ernst, E. 1 Acupuncture for peripheral joint osteoarthritis: A systematic review and meta-analysis. Rheumatology. 2006;45(11):1331-1337

- White, A; Foster, NE; Cummings, M; Barlas, P: Acupuncture treatment for chronic knee pain: a systematic review. 2007 Rheumatology. 46(3):384-390

Physical Medicine and Osteoarthritis: Massage

Whole body massage

Perlman, Adam I. et al: Massage Therapy for Osteoarthritis of the Knee: A Randomized Controlled Trial. 2006 Arch Int Med 166(22):2533-2538, December 11/25,
Treating Osteoarthritis: Nutraceuticals

- Anti-inflammatory agents
  - Boswellia
  - Bromelain
  - Ginger & Curcumin
  - Devil’s claw

- Structural Modification agents
  - Glucosamine / chondroitin
  - SAMe
  - ASU
  - MSM
Boswellia

- Significant improvement over placebo for osteoarthritis of the knee
  - Kimmatkar et al, Ammon et al
- Potentiates effects of glucosamine in experimental conditions
  - Singh et al
- Blocks arachidonic acid - to - leukotriene conversion
  - Poeckel et al
- Standardized to 65% boswellic acids; 300 mg tid
Bromelain

- Sulfur containing enzyme from pineapple plant
- Inhibits PGE2 synthesis
- Enhances PGE1 synthesis
- Decreases vascular permeability
- Separate analgesic properties
- Effective Dosage in studies ranges between 100-900+ mg/day
- No significant adverse effects

Ginger & Curcumin

- Ginger extract on synovial cells
  Frondoza et al 2004

- Ginger Inhibits COX and LOX pathways
  Grzanna et al J Med Food 2005 8(2)125-132

- Ginger ass’ d w/ weakened delayed -type hypersensitivity in mice

- Curcumin as chemopreventive
Harpagophytum procumbens: devil’s claw

- Harpagophytum and low back pain
  - N= 130 treated with H procumbens; significant improvement with no serious side effects
  - Laudahn D Walper A 2001 Phytother Res (15)621-624

- Likely acts synergistically with NSAIDs
  - Brendler T et al J Herb Pharmacotherapy 6(1): 89-126

- COX2 inhibitor
  - Huang et al J Ethnopharmacology 2006; 104:149-155
Structural Modification: Glucosamine Chondroitin

- **GAIT study**
  
  *Clegg DO et al. NEJM 2006;354:795-808*

- **GUIDE study**
  
  *Herrero-Beaumont et al Arth Rheum 2007; 555-67*

- **Meta-analyses**
  
  Towheed TE et al Cochrane Database 2005(2):CD002946
  
  Biggee BA et al Med Health R 2004; 87:176-179
  
  Richy F et al Arch Intern Med 2003; 163:1514-22
Two “definitive” trials

GAIT & GUIDE trials

**GAIT**
(Glucosamine Chondroitin Arthritis Intervention Trial)
Clegg et al 2005 n= 1583
- Glucosamine HCl 500tid vs chondroitin sulfate 400 tid vs combination vs celecoxib 200 qd vs placebo x 24 weeks
- Mild and mod/ severe groups stratified
- Only combination effective in mod/ severe group
- WOMAC scale used
- High placebo rate response (60% )

**GUIDE**
(Glucosamine Unum In Die Efficacy)
Herrero Beaumont et al 2006
- n= 318
- Glucosamine sulfate 1500 mg vs acetaminophen 3000 mg x 24 weeks
- Glucosamine sulfate superior to acetaminophen
- Lequesne 5 pt scale and WOMAC scale used
Glucosamine: Mechanism of action

- Glucosamine is a building block for cartilage
- Glucosamine serum level peaks at 10µm after oral ingestion- thought to be insufficient for clinical effect
- Above 1500 mg dosing, glucosamine serum levels do not rise over 10µm BUT
- Sulfate is increased in serum after oral ingestion
- Serum sulfate concentration is proportional to synovial fluid sulfate concentration
- Glucosamine may act as a carrier for sulfate
- This hypothesis predicts better performance of sulfate vs non-sulfate glucosamine salts

(3) Hoffer LJ. Et al: Metabolism: 2001 (7):767-70
Glucosamine: Mechanism of action

- May inhibit IL-1 signaling cascade and downregulate the catabolic effects of pro-inflammatory molecules present in osteoarthritic cartilage.
  (insert diagram of IL-1 - NF κB activity)
- Inhibits production of matrix metalloproteinase-3, which degrades collagen matrix

Structure modifying effects

- Glucosamine sulfate 1500mg qd x 3 years
- Joint space narrowing over 3 years -3.1 mm with placebo vs 0.06mm with glucosamine
- Five year followup RR of lower limb surgery 0.52 compared to control

Reginster Lancet 2001 357:251-56

- Glucosamine sulfate 1500mg qd x 3 years
- Joint space narrowing over 3 years -0.19 mm with placebo vs 0.04 mm with glucosamine
- Five year followup 75% reduction of knee replacement surgery as compared to control

Dosing for optimum result with glucosamine

- Studies with successful outcomes used higher qd dosing
- Studies with less successful used smaller tid doses
Topical and IM Glucosamine

- Glucosamine more effective than placebo
- Both preparations contained aromatic compounds (camphor or mint)

- **IM**: Glucosamine 400mg 2x/ week vs placebo x 6 weeks
- Response rate 55% vs 33% placebo
- Neither compared to oral glucosamine or NSAID
Some reports of altered glucose metabolism with glucosamine

Biggee et al measured serum glucose and insulin at 15 minute intervals for 3 hours after 75 mg glucose ingestion with and without glucosamine sulfate ingestion

Glucose and insulin serum levels in patients with normal glucose metabolism unaffected

S-adenosyl-L-methionine
SAMe

- As effective as ibuprofen
  
  *Fetrow CW Avila JR Ann Pharmacotherapy 35(11)1414-25*

- Significant improvement over placebo
  
  *Bradley JD et al J Rheumatol 1994; 21: 905-911
  Soeken KL et al J Fam Prac 2002 51:425-430*
Avocado/soybean unsaponifiables

- Byproduct of soapmaking
- In structural-modification category
- Significant improvement over placebo in multiple trials

Arachidonic Acid

Phospholipase A-2

Cyclo-oxygenase Pathway

Lipoxygenase Pathway

Steroids

Leukotrienes

Prostaglandins & Thromboxanes

Aspirin

NSAIDs

COX II Inhibitors: Celebrex, Vioxx, Mobic

Curcumin, Bromelain

Ginger, Devils Claw

Boswellia Turmeric

Colchicine

Sulfasalazine

Leukotriene Inhibitors: Accolate, Singulair, Zyflo

Leukotrienes
Homeopathics

- Topicals: can be useful for all joints, but especially smaller joints
- Injectables: use alone or with smaller dose of cortisol structural-modification category
Allergy/Elimination Diet

- A number of foods commonly found in our diet may cause clinical or subclinical immune reaction in the GI tract, leading to increased intestinal permeability.
- Can contribute to overall increased inflammatory load.
- Manifestations may be in from of overall fatigue, joint and muscle pain, unexplained rash etc.
- Useful in cases of multi-joint pathology.
Allergy/ Elimination Diet

- Foods eliminated: gluten, dairy, eggs, soy, corn, tomatoes, grapefruit, peanuts, processed foods for 3 weeks
- Diet consists of lean meats and fish, all fruits and vegetables except those eliminated, and gluten free grains (rice, quinoa, millet, amaranth, buckwheat)
- Usually given in conjunction with a medical food to calm the GI tract and upregulate liver detoxification
- Foods are added back one by one every 3 days and reactions recorded
Putting it all together

Anti-inflammatory diet
Fat Resistance Diet (Leo Galland MD)
- If weight loss is desired, begin at Stage I
- If weight loss is desired, begin at Maintenance phase

Supplementation
- Combination products
- Intervene at multiple sites: diet/ FA supply/ COX-LOX/ joint modification
- Fish oil daily for at least 6 months, then 5x/week
- May need to try several products for a few weeks each to find best benefit/ side effect ratio
- Most commonly: GI discomfort; reduce by 1/3 and ramp up 1/3 dose per week; treat GI imbalance
WHAT I HOPE I’VE CONVEYED:

- We can think of osteoarthritis as a local manifestation of a systemic process.
- If we treat systemically, the local symptoms resolve more easily.
- Diet has a substantial impact on inflammatory load.
- In addition to an anti-inflammatory diet, anti-inflammatory botanicals, topical and injectable homeopathics, manual therapies and acupuncture are within reach of most physicians to use.
In Conclusion:

1. Osteoarthritis is the result of metabolic dysfunction that manifests in joint dysfunction.
2. Osteoarthritis pain is an example of inflammation-mediated pain.
3. Multiple natural anti-inflammatory compounds exist in nature; and can be accessed through diet.
4. Using an anti-inflammatory diet improves overall health and tissue responsiveness to interventions.
5. Use supplements to intervene at multiple sites in the inflammatory cascade and at joint surfaces.

6. Optimal supplementation may require some trials in materials and dosing.

7. Diet and supplementation create a better substrate for physical medicine and movement modalities such as physical therapy, massage, and acupuncture.

8. Multiple avenues exist for relief of pain and optimization of knee function to support patients in prevention or delay of surgery.
Osteoarthritis: Case Study

Plan:

- Eliminated sugar, gluten and refined food from the diet
- 12 acupuncture treatments
- Physical therapy 2x/ week x 8 weeks for knee soft tissue release and strengthening
- Massage 1x/ week x 4 weeks, then monthly
- Supplements: 3g DHA/ EPA qd; anti-inflammatory herbal combination (bromelain, ginger, curcumin, ); glucosamine 1500 mg/ day
- Home exercise program
Patricia McDonough has successfully avoided surgery and has controlled her pain without medication

- Follows anti-inflammatory diet
- Does occasional weeks as vegan
- Gets massage 1-2x/month
- Continues to take supplements
- Returns for short course of acupuncture when pain returns
- Recently told by Orthopedist that joint space in her knee has increased
THANK YOU
Integrative Medicine Treatment of Osteoarthritis

Questions for discussion:

- Is it plausible that diet is as powerful as pharmaceutical agents in treatment of OA?
- What, if any, is the relationship between joint health and gut health?
- Is gluten sensitivity the same as celiac disease?
- How do you think the economics of OA treatment change with widespread use of the modalities described?
- Weight loss has previously been used as a strategy to unload OA joints. Since fat tissue stores inflammatory cytokines, research the link between decreased fat tissue and decreased inflammatory load.
1. Assess structure, nutritional status, inflammatory load,
2. Decrease inflammatory load through diet
3. Modify aggravating structural imbalances: tight muscles, tendons and joint capsules, postural defects, muscle weaknesses
4. Restore energy movement and balance
5. Add anti-inflammatory nutraceuticals and intervene at as many sites as possible
6. This is a baseline approach to chronic inflammation-based pain
   Osteo- and Rheumatoid arthritis
   Fibromyalgia
   Chronic muscular pain
   Neurodegenerative pain
   Peripheral vascular pain