

Alternative Therapies in Inflammatory Bowel Disease

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Children IBD Center Lecture Series April 7, 2005

What is Alternative Medicine?

- Any form of medicine that is outside the mainstream of western or conventional medicine practiced by most doctors
- Term is loosely used to cover all forms of medicine except allopath
- 1973, the Medical Faculty of the Univ. of Rome convened the first World Congress of Alternative Medicines - provisional program contained 135 therapies

Allopathy: The system of medical practice which treats disease by the use of remedies which produce effects different from those produced by the disease under treatment. MDs practice allopathic medicine

The term "allopathy" was coined in 1842 by C.F.S. Hahnemann to designate the usual practice of medicine (allopathy) as opposed to homeopathy, the system of therapy that he founded based on the concept that disease can be treated with drugs (in minute doses) thought capable of producing the same symptoms in healthy people as the disease itself.

Alternative Medicine:

- Exists in all cultures to some degree
- Includes terms such as traditional medicine, indigenous medicine or folk medicine
- Dates back hundreds and thousands of years
- Different regions, different disciplines
- Chinese - acupuncture
- French - magnetic healing
- German - Heilpraxis
- English - Herbalism
- India - Ayurveda with Siddha
- Japan - Shiatsu

Most Popular Forms of Alternative Medicine:

Ayurveda

Herbalism
Homeopathy
Meditation
Naturopathy
Aromatherapy
Yoga
Bach Flower Remedies
Acupuncture
Chromo therapy
Acupressure
Diet therapy
Magneto therapy
Hydrotherapy
Shiatsu
Reiki

Complementary and alternative medicine (CAM) used by Canadian patients with inflammatory bowel disease

Hilsden RJ, Verhoef MJ, Best A, Pocobelli G. Am. J Gastroenterology. 2003 Jul; 98(7): 1563-8.

- Postal survey of the members of the Crohn's and Colitis Foundation of Canada; gathered data on demographics, disease, conventional IBD treatment and on the use and perceived effects of CAM
- Respondents were characterized as not using CAM, as past or present users of CAM for their IBD, or as present users of CAM for other reasons
- Final sample included 2847 IBD patients
- Current or past use of CAM for IBD was reported by 1332 patients, of whom 666 continued their use of CAM
- Only 15% used CAM before their IBD diagnosed
- Improvements in sense of well-being, IBD symptoms, and sense of control most commonly reported benefits
- 46% had spent more than \$250/yr

National Center for Complementary and Alternative Medicine:

- Understanding Complementary and Alternative Medicine
- Major areas of CAM
- Alerts and Advisories

- Treatment Information
- Dietary and Herbal Supplements

<http://nccam.nih.gov>

10 Things to Know About Evaluating Medical Resources on the Web:

1. Who runs the site?
2. Who pays for the site?
3. What is the purpose of the site?
4. Where does the information come from?
5. What is the basis of the information?
6. How is the information selected?
7. How current is the information?
8. How does the site choose links to other sites?
9. What information about you does the site collect, and why?
10. How does the site manage interactions with visitors?

Role of oxygen free radicals in the etiology of pouchitis.

Levin KE et al. Dis Colon Rectum. 35:452-6; 1992

- Transient mucosal ischemia may cause oxygen free radical production by xanthine oxidase, precipitating pouchitis after ileal pouch-anal anastomosis
- 8 patients with acute pouchitis were treated with allopurinol during the episode while 14 treated with antibiotics
- 50% of each group responded

Antioxidant effects of herbal therapies used by patients with inflammatory bowel disease: an in vitro study.

Langmead C et al. Alimentary Pharmacology & Therapeutics 16:197-205; 2002

- Reactive oxygen metabolites (ROM) are present in excess in inflamed colonic mucosa
- Antioxidant actions of aminosalicylates (5-ASA) may constitute part of their therapeutic effect
- Novel drugs or therapies for IBD that have antioxidant activity may be useful clinically
- Many herbal concoctions are said to be effective in inflammatory conditions; little clinical & pharmacological data to support

- Aim to investigate the antioxidant effects in vitro of six herbal remedies

1. Slippery elm - derived from the bark of the slippery elm tree
2. Fenugreek - an Ayurvedic therapy
3. Mexican yam - a tropical staple
4. Devil's claw - the root of an African flower
5. Tormentil - a European flower
6. Wei tong ning - a traditional Chinese herbal therapy

Tested the antioxidant effects of each of these herbal preparations in two cell-free radical generating systems and one biological system:

- Xanthine/xanthine oxidase for superoxide
- Phycoerythrin degradation assay for the peroxy radical
- Inflamed colorectal mucosal biopsies, using 5-ASA as a positive control and orange juice as a nontherapeutic phytic control

RESULTS:

- Slippery elm, Mexican yam, Devil's claw, tormentil, Wei tong ning and 5-ASA all had dose-dependent antioxidant effects
- Fenugreek and orange juice had no effects except undiluted
- The potency for each herb ranged 100 fold

Phycoerythrin degradation assay

- All the herbs and 5-ASA had dose-dependent peroxy-radical scavenging effects-1,000 fold difference based on concentrations

Inflamed colorectal biopsies

- Chemiluminescence (reaction that produces light by certain bacteria or fungi) was significantly reduced in biopsies incubated with slippery elm, fenugreek, Devil's claw, Wei tong ning, and tormentil
- There was no significant antioxidant effect with Mexican yam or orange juice

CONCLUSION:

- In vivo, antioxidants may exert their activity at several different points in the pathways of oxidant metabolism
- Prevention of radical generation may be achieved at a tissue level as a result of down-regulating of recruitment and/or activation of neutrophils or monocytes

What is Ayurveda?

Ayurveda is a holistic science of wellness based on creating harmony between two fundamental complementary forces, movement, observed in respiration, circulation, digestion, elimination and in the nervous system, and stability which provides the structure to support movement. Behind these two forces is the one energy which makes it all happen. Ayurveda works through keeping these forces in balance, which creates harmony with this natural rhythm found in all life. Harmony reflects itself in wellness just as all disease grows from an imbalance.

Trichuris suis therapy in Crohn's Disease

Summers RW et al, Gut. 2005; 54:87-90

- Crohn's is common in parts of the world where round worm infection is rare and uncommon in those areas where most people carry worms
- It appears to result from an inappropriate immune response to normal gut flora
- Round worms lower the immune response to outside proteins, which could be beneficial in Crohn's disease
- Round worms reduce inflammations in experimental animal colitis
- Trichuris suis, the pig whipworm, is similar to human whipworm *T trichiura*
- Ingestion of *T suis* ova results in short term self limited colonization of the host intestine
- 24 week clinical trial conducted to evaluate the safety and possible efficacy of live *T suis* therapy in Crohn's disease

Eligible patients and methods:

- 29 patients with active CD defined as Crohn's disease activity index (CDAI) 220-450
- All patients drank 2500 live *T suis* eggs every 3 wks for 24 wks
- Remission was defined as a decrease in CDAI < 150 while a response was defined as a decrease in CDAI of >100

Trichuris suis therapy in Crohn's disease: bottom line:

- By 12 and 24 weeks, $\frac{3}{4}$ of patients had either responded or were in remission

Acupuncture and Moxibustion in the Treatment of Active Crohn's Disease: A Randomized Controlled Study

Joos S et al. Digestion. 2004;69: 131-9

- Randomized controlled study in patients with active CD investigating the efficacy of traditional acupuncture by assessing disease activity using an established scoring system and by evaluating quality of life, subjective well-being and serum markers of inflammation
- All patients with CDAI (Crohn's Disease Activity index, higher numbers correlate with increase in disease activity) between 150-350, stable medications, no immunomodulators
- All patients received 10 acupuncture sessions of 30 minutes each over a period of 4 weeks
- All patients were treated in the sitting position at the back points for 10 minutes
- In TCM group, needles were inserted 0.5-3cm and manipulated by hand and treated with moxa burned sown in a wooden box positioned on the abdomen
- In control group so-called minimal acupuncture was performed, meaning that needles were placed away from the classical or trigger points (non-acupoints) and inserted only 1-2mm deep

RESULTS:

- In the patient group receiving acupuncture according to TCM principles, there was a significant fall in mean CDAI after treatment, which remained fairly stable in the follow-up period
- Changes in the quality of life evaluation did not reach a significant difference ($p=0.064$), since IBDQ score improved in both groups

Mycobacterium and Crohn's

- Pathological and clinical similarities between animal paratuberculosis, intestinal tuberculosis, and Crohn's
- Paratuberculosis, also known as Johne's disease, is a chronic enteritis that affects cattle and other species and is caused by Mycobacterium avium subspecies paratuberculosis (MAP)
- Early studies did not detect MAP in tissues from patients with Crohn's disease by conventional staining and culture techniques

Culture of *Mycobacterium avium* subspecies *paratuberculosis* from the blood of patients with Crohn's

Naser SA, Ghobrial G, Romero C, Valentine JF. *Lancet*, 2004; 364:1039-44

- Blood obtained to do PCR on buffy coat for MAP, DNA as well as culture for MAP
- 52 subjects participated: 28 with Crohn's, 9 with UC, 15 controls

Implications of Positive MAP Testing

- Implies that there may indeed be an infectious cause to Crohn's
- Recent research into Nod2 (genetic) testing may indicate that certain individuals are susceptible to bacterial infection/inflammation
- May provide other avenue of treatment, i.e. anti-TB drugs

Treatment of ulcerative colitis with fish oil supplementation: A prospective 12 month randomized controlled trial

Hawthorne Ab et al, *Gut*. 1992 Jul;33(7):922-8

- 87 patients received supplements HiEPA fish oil as triglyceride (4.5 g of eicosapentaenoic acid) or olive oil placebo for one year
- oils given in addition to standard drug therapy
- Fish oil significantly increased the eicosapentaenoic acid content of rectal mucosa
- Associated with increased synthesis of leukotriene B5, and 53% suppression of leukotriene B4 synthesis stimulated neutrophils
- Treatment with fish oil resulted in measurable, but only limited clinical benefit
- For patients entering the trial in relapse (n=53), there was a significant reduction in corticosteroid requirement after 1&2 months of treatment
- For patients in remission at trial entry or during the trial (n=69), there was no significant difference in the rate of relapse
- Conclude that fish oil produces a modest sparing effect in active disease, but no benefit in maintenance therapy
- 4-mo treatment periods (fish oil and placebo) separated by 1-mo washout
- 24 patients with active UC entered - 5 dropped out and 1 was

noncompliant, 18 completed the study, all with active disease

- Treatment with prednisone and sulfasalazine continued
- Fish oil supplementation consisted of 18 MAX-EPA capsules daily (eicosapentaenoic acid, 3.24 g; and docosahexaenoic acid, 2.16g)
- Placebo supplementation consisted of 18 identical capsules containing isocaloric amounts of vegetable oil
- Evaluations included a review of systems, flexible sigmoidoscopy, rectal biopsy, and rectal dialysis to measure prostaglandin E2 and leukotriene B4 levels

RESULTS:

- Fish oil supplementation resulted in a significant decrease in rectal dialysate levels of leukotriene B4
- Significant improvements were seen in acute histology index and significant weight gain
- No significant change in variable during the placebo period
- 7 patients received concurrent treatment with prednisone and during the fish oil supplementation period, the mean prednisone dose decreased from 12.9 mg/d to 6.1 mg/d and rose from 10.4 mg/d to 12.9 mg/d during the placebo diet period (P greater than 0.20)

CONCLUSIONS:

- Four months of diet supplementation with fish oil in patients with inflammatory bowel disease resulted in reductions in rectal dialysate leukotriene B4 levels (produces inflammation), improvements in histological findings and weight gain