

Integrative Pain Management

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Collaborative Cancer Care Symposium

Bozeman, MT, September 20, 2008



Cancer and Pain

- Pain can cause:
 - Discontinuation of treatment
 - Malnutrition
 - Depression
- 34% of cancer patients experience neuropathic pain
- 60% of adults with newly diagnosed or intermediate-stage cancer
- 95% of patients with advanced disease
- But less than 50% of patients experience effective pain relief with conventional medical interventions



Communication is Key

- Communicating about pain can be difficult
- Non-compliance with treatments affect outcomes
- Pain rating scales
- Pain diary



Important Pain Symptoms

- Location
- Frequency
- Intensity
- Duration
- Radiation
- What makes it worse
- What makes it better



Patient as Advocate

- Pain, medical terminology, emotional distress, medications impair ability to retain information
- Therefore:
 - Advocate for yourself
 - Bring someone along to advocate for you
 - Request information written down
 - Request information given in small chunks



Most Effective Strategy

- Pharmacologic *plus* nonpharmacologic strategies
- Pharmacologic
 - Opioid analgesics
 - Anesthetics
 - Etc.
- Non-pharmacological
 - Acupuncture
 - Botanicals
 - Cognitive Behavioral Therapy
 - Nutrients
 - Massage
 - Meditation
 - Reflexology

Calendula for Radiation-Induced Dermatitis

(J Clin Oncol 2004;22:1447-53)

- Topical calendula (*Calendula officinalis*) ointment
- Comparison medication: Trolamine
- Phase III randomized trial
- Twice daily or more for 8 months
- Patients: 254 women (ages 18-75 years) with breast cancer who received postoperative radiation therapy
- Calendula group: 41% of women experienced Grades 1 or 2 dermatitis, and 7% Grade 3
- Trolamine: 63% experienced Grades 2 or 3, 20% Grade 4
- Pain scores were \approx 75% less with calendula vs. Trolamine

Glutamine for Chemo-Induced Oral Mucositis

(Cancer 1998;83:1433-9)

- 24 patients (16 children, 8 adults)
- Sarcoma (Ewing's Osteosarcoma, Rhabdomyosarcoma): 11 patients
- Neuroblastoma: 1 patient
- Chemo:
 - CAD(Cyclophosphamide, doxorubicin, dacarbazine)
 - VAdrC (Vincristine, doxorubicin, cyclophosphamide)
 - IA (Ifosfamide, doxorubicin)
 - CDDPAdr (Cisplatin, doxorubicin)
 - MTX (high dose methotrexate)

Glutamine for

Chemo-Induced Oral Mucositis

- Design: Randomized, placebo, double-blind, crossover over four courses of chemotherapy
- Medication: 2 grams oral glutamine suspension or glycine placebo daily
- Duration: The day of chemotherapy treatment and for 14 days after
- Swish and swallow in the morning and evening

Glutamine for

Chemo-Induced Oral Mucositis

- Results: Severity and duration of mucositis decreased
- Mucositis duration was 4.5 days less in treatment group
- Duration of severe painful mucositis requiring that the patient's diet be modified to soft foods was 4 days less with glutamine

Magnesium for Treatment of Neuropathic Pain

(J Pain Symptom Manage 2000;19:35-39)

- Neuropathic pain: up to 34% of cancer patients
- Magnesium:
 - muscle relaxant
 - NMDA-receptor antagonist
- I.V. Magnesium Sulfate (500 mg or 1 gram)
- 12 patients (7 men, 5 women), avg age 63 years



Magnesium for Treatment of Neuropathic Pain

- All with neuropathic pain due to cancer in the brachial and lumbosacral plexus
- Patients were poorly responsive to opioid analgesics (mean morphine dose was 200 mg)
- Opioid medication was not discontinued
- I.V. 1 mL (500 mg) or 2 mL (1 g) magnesium sulfate over 5 to 10 minutes
- Within one hour after immediate-release opioid preparation or 4 hours of extended-release preparation



Magnesium for Treatment of Neuropathic Pain

- Results of 500 mg infusion
- 3 patients had complete resolution of pain
- 2 patients had partial resolution of pain
- 1 patient had no relief
- Improvement began 15 minutes after infusion; maximum benefit was at 45-60 minutes
- Duration of improvement: up to 4 hours

Magnesium for Treatment of Neuropathic Pain

- Results of 1 gram infusion
- 1 patient had complete resolution of pain
- 4 patients had partial resolution of pain
- 1 patient had no relief
- Improvement began 15 minutes after infusion; maximum benefit was at 60 minutes
- After 4 hours:
 - 2 patients reported continued analgesic effect
 - 2 patients reported pain beginning to return
 - 1 patient reported pain had fully returned

ALA for Treatment of Oxaliplatin-Induced Polyneuropathy

(J Clin Oncol 2002;20:3359-3361)

- Alpha lipoic acid (ALA)
- Dose-limiting toxicity of oxaliplatin is cumulative peripheral sensory neuropathy (PNP)
- PNP symptoms:
 - Paresthesias with or without functional impairment of the extremities
 - Develop in 10-18% of patients when a cumulative dose of about 800 mg/m² is reached



ALA for Treatment of Oxaliplatin-Induced Polyneuropathy

- 15 patients with oxaliplatin –induced cumulative PNP
- Treatment:
 - Alpha-lipoic acid 600 mg I.V. weekly for 3-5 weeks
 - Followed by 600 mg orally three times daily until full recovery or for a maximum of 6 months
- 8 of 15 patients (53%) experienced reduction in severity of symptoms
- Median response time: 4 weeks (range 3-12 wks)
- Median treatment duration: 2 months (range 1-4 months)

Ca/Mg for Prevention of Oxaliplatin-Induced Polyneuropathy

(Clin Cancer Res 2004;10(12):4055-4061)

- Oxaliplatin neurotoxicity may result from chelation of magnesium and calcium
- Retrospective analysis of 161 patients (96 received infusions of Ca/Mg) before and just after oxaliplatin treatment).
- Calcium gluconate 1 g and magnesium sulfate 1g I.V. over 15 minutes just before and after oxaliplatin infusions
- Withdrawal due to neurotoxicity: 4% in Ca/Mg group vs. 31% in control
- Neuropathy: 20% in Ca/Mg vs. 45% in control

Ca/Mg for Prevention of Oxaliplatin-Induced Polyneuropathy

- At end of treatment: severe chronic neuropathy was present in 8% of Ca/Mg group vs. 20% in control
- No significant differences in tumor response rate between groups
- Acute symptoms were much less frequent and severe in Ca/Mg group
- Recovery from neuropathy was quicker in Ca/Mg group

Vitamin E for Prevention of Cisplatin Neurotoxicity

(J Clin Oncol 2003;21:927-931)

- Neurotoxicity is the major dose-limiting toxicity for cisplatin
- Peripheral sensory polyneuropathy, ototoxicity, focal encephalopathy
- Signs and symptoms often not reversible
- Mechanism of toxicity not fully understood
- Mechanisms: free radical damage to nerves; possible vitamin E depletion

Vitamin E for Prevention of Cisplatin Neurotoxicity

- Medication: Vitamin E as alpha-tocopherol
- Dose: 300 mg (447 IU)/day
- Protocol: Vitamin E administered before cisplatin therapy and continued for 3 months after cessation of cisplatin treatment
- Patients were randomized to receive vitamin E plus cisplatin (Group 1) or cisplatin alone (Group 2)
- Median time between start of vitamin E and cisplatin was 4 days (range, 1 to 8 days)

Vitamin E for Prevention of Cisplatin Neurotoxicity

- 27 patients with solid tumors (15 lung; 3 ovarian; 2 rhinopharinx, ; 2 urethral; and 1 each gastric, testicular, esophageal, ethmoidal, tongue) completed six cycles of cisplatin therapy
- Neurotoxicity: Group 1 was 30.7% vs. 85.7% in Group 2
- Severity of neurotoxicity was 79% less in Group 1 compared to Group 2
- Overall there was a 64% decreased risk in developing neurotoxicity with Vitamin E
- No differences between groups in response to cisplatin treatment were noted (eg, tumor weight inhibition, tumor growth delay, life span)



Customized Approach

- Biochemical testing
- What is biochemistry?
 - Vitamins
 - Minerals
 - Amino acids (eg, glutamine--decreased in patients with cancers of the head, neck, breast, GI tract)
 - Fats
- Symptoms are biochemical



Case 1: Breast Cancer

- 54 year old woman with breast cancer
- She underwent a radical mastectomy, radiation and chemotherapy
- Chief complaints:
 - severe indigestion
 - insomnia
 - constipation
 - muscle aching and spasms
 - severe fatigue (four out of ten, with ten being best)



Biochemical Testing Revealed

- Severe amino acid deficiencies, suggesting damage to the intestines and malabsorption (including low glutamine)
- Low minerals (chromium, copper, magnesium, selenium, zinc)
- Low omega-3 series polyunsaturated fatty acids, which are anti-inflammatory
- Decreased ability to burn fat for energy; functional deficiency in L-carnitine
- Decreased ability to use carbohydrates for energy; functional deficiencies in vitamins B1, B3, lipoic acid and CoQ10
- Specific indicators for functional deficiencies in vitamins B1, B2, B3, B5, B6 and B12
- Multiple intestinal infections, including *Clostridia* spp. and yeast (*Candida* spp.)
- Food allergy to egg whites



Case Results

- She was placed on a therapeutic program tailored specifically to her needs, which included diet and nutraceuticals.
- Over the next several months her muscle cramps, indigestion and constipation completely resolved, and her energy increased to eight out of ten (ten being best).
- Moreover, she described a general increase in vitality and strength.
- [Click to view test results](#)

Case: Large Granulomatous Leukemia

- 72 year old man diagnosed with hypercellular marrow with T-cell lymphoproliferative disorder consistent with T-Cell Large Granular Lymphocyte Leukemia (T-LGL Leukemia) based on an iliac bone marrow aspiration and biopsy.
- He also had past diagnoses of insulin dependent diabetes mellitus (IDDM) and hypertension.
- Chief complaints:
 - Low energy (one out of ten with ten being best)
 - weight loss of 30 pounds in past three months



Biochemical Testing Revealed

- Amino acid deficiencies
- Free radical damage to DNA (risk factor for cancer)
- Low minerals
- Decreased ability to burn fats and sugars for energy
- Functional B-complex vitamin deficiencies
- And more...[Click to see test results.](#)



Case Results

- Energy improved to eight out of ten with ten being best
- Weight increased by fifteen pounds
- He was able to go fishing again



Summary

- An integrative approach to pain yields the best results
- Assemble your team
- Helpful therapies include:
 - Vitamin E
 - Alpha Lipoic Acid
 - Glutamine
 - Calendula ointment
 - Intravenous Magnesium and Ca/Mg
- Biochemical testing may provide additional benefits