Managing the Physical and Emotional Side Effects Throughout Treatment

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Overview

• New cases (2014): 232,670
• % of all new cancer cases: 14.0%
• Percent surviving 5 years (2004-2010): 89.2%

Overview

• Death rates have been falling on average 1.9% each year for the years 2002-2011

Overview

• The overall treatment effect: “I’m fine, really. I cry only when I come to see you.”

• The chemotherapy effects: “I was an active, energetic person and now I feeling like a hurting blob.” AND “I am not as sharp as I was.”

• The anti-estrogen effect: “I feel like a 50 year-old in an 80 year-old body.” AND “There was a darkness there that lifted.”
Overview

- “I’m fine, really. I cry only when I come to see you.”
- “I was an active, energetic person and now I feeling like a hurting blob.”
- “I am not as sharp as I was.”
- “I feel like a 50 year-old in an 80 year-old body.”
- “There was a darkness there that has lifted.”
- Post-traumatic stress disorder
- Chemotherapy-induced neuropathy
- Chemo-brain
- Aromatase inhibitor-induced arthralgias
- Anti-estrogen-induced cognitive and emotional changes
PTSD: “I’m fine, really. I cry only when I come to see you.”
PTSD: overview

• Intrusive thoughts
• Avoidance
• Negative changes in thinking or mood
• Changes in emotional reactions
PTSD: overview

• 3-4% prevalence at time of diagnosis for all cancer types
• 35% prevalence after treatment for all cancer types

http://www.cancer.gov/cancertopics/pdq/supportivecare
PTSD: breast cancer specifics

• ~25% of newly diagnosed women with breast cancer are reported to have PTSD.
• 15-35% persistent PTSD
• African american, asian and younger women had higher rates of PTSD
• 3 or more axillary LNs more likely, prior medical illness, prior psychological illness were risk factors


O'Connor, et al How traumatic is breast cancer? Post-traumatic stress symptoms (PTSS) and risk factors for severe PTSS at 3 and 15 months after surgery in a nationwide cohort of Danish women treated for primary breast cancer, Br J Cancer, 2011 Feb 1

PTSD: breast cancer specifics

• Predictable time points
  • Hearing the diagnosis
  • Limbo points
• The “Cliff Effect”
• The “Oncology Appointment Effect”
PTSD: treatments

- Recognition
- Counseling, medication, support groups
Chemotherapy-induced neuropathy: “I was an active, energetic person and now I feeling like a hurting blob.”
Chemo-induced neuropathy: overview

- Stocking glove distribution, symmetric, starts distally and moves upward
- Affects sensory but not motor function
- Risk factors: dose effect
Chemo-induced neuropathy: treatments

• Treatments:
  • Duloxetine trial
  • Other medications
  • Acupuncture
  • ?Acetyl-L-Carnitine

• ?Prevention
Chemo-induced neuropathy: treatments

• Duloxetine trial: randomized, placebo controlled
• 231 patients, pain ratings over 5 weeks
• Those on duloxetine had better relief of pain than placebo

Smith, et al. Effect of duloxetine on pain, function, and quality of life among patients with chemotherapy-induced painful peripheral neuropathy: a randomized clinical trial., JAMA. 2013 Apr
Chemo-induced neuropathy: treatments

[Graph showing percentage of patients (%) with pain reduction from baseline to endpoint of initial treatment period for Duloxetine and Placebo]
Chemo-induced neuropathy: treatments

• Other medications
  • Gabapentin
  • Tricyclic anti-depressants (nortriptyline)
  • Opiates
  • B vitamins
  • ? Acetyl-L-Carnitine
Chemo-induced neuropathy: treatments

- Acupuncture trial: randomized, placebo controlled
- 90 patients
- True acupuncture vs sham acupuncture (needle insertion where no electrodermal signal detected)
- True acupuncture group reported 36% reduction in pain intensity at 2 mos vs 2% reduction in placebo group

Chemo-induced neuropathy: ?prevention

• ASCO Guidelines for prevention
  • What NOT to do (!):
    • Acetly-L-Carnitine
    • Ca-MG infusions
    • Glutathione
    • Vit E

Chemo-induced neuropathy: prevention

- Acetyl-L-Carnitine Prevention Trial: Randomized, placebo-controlled
- 400 women getting adjuvant taxane-based chemotherapy
- ALC 3000mg daily vs placebo
- no difference at 12 weeks
- worse neuropathy in treatment arm at 24 weeks

Chemo-brain: “I’m not as sharp as I was.”
Chemo-brain: overview

• Word recall
• Trouble concentrating
• Trouble multi-tasking
• Longer time to complete tasks
• Etiology unknown, association with high dose chemo
• Differences in brain appearance and function on imaging
Chemo-brain: overview

- Other culprits besides chemotherapy
- Observational study:
  - 70 women with breast cancer, getting AC and also T
  - Evaluated at time of diagnosis, after completion of AC, and then 6 months after completion of all chemo
  - 23% had cognitive dysfunction at time of diagnosis
  - Decreases various aspects of cognitive dysfunction during chemo, with improvement by 6 months after chemo

Chemobrain: treatment

• Area of clinical trial interest
  • Nicotinic Treatment of Post-Chemotherapy Subjective Cognitive Impairment: A Pilot Study, NCI
    • Randomized, placebo controlled
    • Women with stages 1-3A breast cancer, who have undergone chemotherapy in last 1-5 years
    • Transdermal nicotine patch x 6 weeks

• Mental rehearsal, behavioral changes
Aromatase inhibitor-induced arthralgias (AIA): “I feel like a 50 year-old in an 80 year-old body.”
AIA: overview

• Symmetric, hands, wrists, knees, can also be migratory
• Trigger finger and carpal tunnel complaints also seen
• Stiffness, decreased grip strength, muscle aches
• Median time to onset is 1.5 months, peaks around 6 months
• Incidence for those experiencing this side effect is thought to be around 50% (some trials show lower, but weren’t designed to look for this)
AIA: overview

- Risk factors:
  - BMI <25 or >30
  - prior HRT
  - prior chemotherapy (perhaps specifically a taxane)
  - ? preceding OA (only one study showed that this increased the risk)

- Etiology unknown
  - lower estrogen levels are linked with higher inflammatory cytokine levels

AIA: overview

• Drop-out rates ~15% after 12 months, and rates of 30-40% have been reported 3 years out

• Do side effects correlate with lower risk of recurrence?

AIA: treatments

- Treatments:
  - Acupuncture
  - Exercise
  - Switching medications
AIA: treatments

• Acupuncture
• ~40 women enrolled for acupuncture twice weekly x 6 weeks. True acupuncture vs sham acupuncture (superficial needle insertion at non-significant locations)
• Pain rated on scale from 1-10, (5-6 starting point)
• 80% in TA group reported 2 point reduction at 6 weeks vs 22% for SA group, statistically sig

Crew et al, “Randomized, Blinded, Sham-Controlled Trial of Acupuncture for the Management of Aromatase Inhibitor–Associated Joint Symptoms in Women With Early-Stage Breast Cancer”, JCO, March 1 2010
AIA: treatments

• Exercise: The HOPE Study

• 121 women, previously inactive, overweight

• randomly assigned to exercise (150 minutes per week of aerobic exercise and supervised strength training twice per week) or usual care over 12 months

• At 12 mos, almost a 30% point decrease in worse pain score for women in exercise group vs 3% increase for women in usual care

Irwin, et al "Randomized Exercise Trial of Aromatase Inhibitor–Induced Arthralgia in Breast Cancer Survivors" JCO, December 1, 2014
AIA: treatments

• Tolerance of alternate AI
• 179 patients enrolled
• Started letrozole after 1 month washout period off arimidex.
• At 6 months 70% of patients were able to tolerate letrozole. And on average mean pain score was 20% lower than when they had been on arimidex.

Briot et al, “Effect of a switch of aromatase inhibitors on musculoskeletal symptoms in postmenopausal women with hormone-receptor-positive breast cancer: the ATOLL (articular tolerance of letrozole) study” Breast Cancer Res Treat 2010
Anti-estrogen-induced cognitive and emotional changes: “There was a darkness there that has lifted.”
Anti-estrogen therapy effects: overview

• Cognitive effects
• Emotional effects
• Conflicting information on whether there is an effect and which class of anti-estrogens is associated with a worse effect
Anti-estrogen therapy effects: overview

• Estrogen receptors in the brain
• STAR trial: tamoxifen associated with slight worsening of depression after starting, which then returned to baseline after 6 months
• Case reports for severe mood disturbances after initiation of AIs, but no identifiable trend
Questions?