Non-Drug Treatment Approaches For Chemotherapy Neuropathy

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# Faculty Disclosure

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- No, nothing to disclose
- Yes, please specify:
Objectives

• To discuss currently available non pharmacologic treatment options for chemotherapy induced neuropathy
• To discuss future research strategies of non pharmacologic modalities.
Outline

• Introduction
• Cancer rehabilitation
• Exercise and Balance Training
• Integrative therapies: Acupuncture
• Neuro-stimulatory options
• Future Strategies
Introduction: Chemotherapy Induced Neuropathy (CIPN)

- Management Challenges
  - Insufficient understanding of mechanisms involved
  - Limited efficacy of traditional treatments
  - Pharmacologic interventions can have toxicities
  - Inadequate management of functional / whole body effects of CIPN
CIPN Effects are Not Solely Peripheral

• Functional impairments are common and are multifaceted
  – Gait and balance effects
  – Peripheral effects
  – Central effects
  – Neurocognitive effects
CIPN Associated Functional Deficits

Winters-Stone, et al JCO 2017
CIPN and Early Balance Changes

Monfort, SM..., Loprinzi, CL, Chaudhari, A Lustberg MB. Breast Cancer Research and Treatment, 2017
Role of non-pharmacologic interventions

Cancer Rehab

Exercise and Balance training

Pharmacologic options

New modalities under study (Scrambler; acupuncture others)

RESEARCH!

www.mascc.org/meeting
Outline

• Introduction
• **Cancer rehabilitation**
• Exercise and Balance Training
• Integrative therapies: Acupuncture
• Neuro-stimulatory options
• Future Strategies
Cancer Rehabilitation

- Restore functional capacity
- Primary prevention of disability
- Reducing impairment and disability
- Improve quality of life
- Foster independence
Cancer Rehab and CIPN

• Functional physical examination for gait and balance evaluation
  – Coordination
  – Proprioception
  – Strength
  – ROM
  – Balance
  – Transfers
  – Gait

Functional in office assessment

- Timed Get Up and Go test
- Berg Balance Scale
  • 14 item scale out of 56 points
  • Identifies low, medium, or high fall risk
- Six minute walk test
Outline

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Exercise Clinical Data

- Kleckner et al.: Phase III randomized controlled trial
  - 355 patients beginning taxane-, platinum-, or vinca alkaloid-based chemotherapy
  - Assigned to Chemotherapy or Chemotherapy & Exercise for Cancer Patients (EXCAP)
    - Standardized, personalized, moderate-intensity home-based 6-week progressive walking and resistance exercise program

Kleckner, I.R., Kamen, C., Gewandter, J.S. et al.
Exercise Clinical Data

• Kleckner et al.: Results
  – Exercise protocol reduced CIPN symptoms of hot/coldness in hands/feet (−0.46 units, p = 0.045) compared to control
  – Exercise intervention reduced numbness and tingling (− 0.42 units, p = 0.061) compared to control
Are there ways to make exercise for CIPN more appealing?
Emerging Exercise Modalities

- The art form of dance is particularly promising for functional rehabilitation
- provides an opportunity to practice balance and gait with cognitive problem solving (i.e., dual-tasking) in regard to spatial navigation
- Social interaction!
Exercise & Balance Training: Clinical Data

- Cancer survivors with neuropathy and postural control deficits at baseline
- Attended Tango classes

Worthen-Chaudhari, L., Chaudhari, A, Lustberg, MB et al. 2018
Exercise & Balance Training: Mechanism

- Exact mechanisms are still under study
- May treat CIPN through changes in inflammation and sensory pathways in the brain
- Exercise-induced changes in the brain may counteract central sensitization associated with neuropathic pain and reduce CIPN symptoms
- Preclinical and clinical studies are in process

Kleckner, I.R., Kamen, C., Gewandter, J.S. et al.
Exercise and Balance Training: Future Directions

- Evaluate generalizability of findings to more severe CIPN patient populations
- Improve adherence with social / art based techniques
- Learn about optimal dose of exercise (type, duration, and intensity)
- A personalized exercise prescription tailored to patient and drug regimen
Outline

- Introduction
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Acupuncture and CIPN

- Absences of phase III randomized data in acupuncture and neuropathy
- Many patients are seeing services
- Small studies have been completed with some promising results
Acupuncture: Clinical Data

• Bao T. et al.: single arm prospective clinical trial pilot study
  – 27 multiple myeloma patients after Bortezomib treatment
  – Reported CIPN ≥ grade 2 at baseline
  – Received 10 acupuncture treatments for 10 weeks (2×/week for 2 weeks, 1×/week for 4 weeks, and then biweekly for 4 weeks)
  – Outcome measures assessed with the Clinical Total Neuropathy Score (TNSc), Functional Assessment of Cancer Therapy/Gynecologic Oncology Group–Neurotoxicity (FACT/GOGNtx) questionnaire, and the Neuropathy Pain Scale (NPS)

(Bao T., Goloubeva O, Pelser C, et al. 2014)
Acupuncture: Clinical Data

(A) Change in FACT/GOG-Ntx scores over 14 weeks. FACT/GOG-Ntx scores at each time point (means and 95% confidence intervals). (B) Change in NPS scores over 14 weeks. NPS scores at each time point (means and 95% confidence intervals).

(Bao T, Goloubeva O, Pelser C, et al. 2014)
Acupuncture point location map. Acupuncture needles were inserted 0.5 to 2 inches into the skin to reach *de qì* sensation and remained in the skin for 20 minutes.

(Bao T, Goloubeva O, Pelser C, et al. 2014)
Integrative Therapies During and After Breast Cancer Treatment: ASCO Endorsement of the SIO Clinical Practice Guideline

• Insufficient evidence for omega 3 fatty acids, vitamin E, acupuncture for treatment of CIPN
• Acetyl-L-carnitine is **NOT** recommended to prevent CIPN
Acupuncture: Future Directions

- Determine the precise mechanism of acupuncture
- Complete large, randomized, controlled trials of acupuncture to treat CIPN among cancer patients
- Development of best practice guidelines

**Bottom line:** currently insufficient data to recommend acupuncture for treatment of CIPN (ASCO/SIO, 2018)
Outline

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• **Neuro-stimulatory options**
• Future Strategies
Neurostimulatory options and CIPN

- Transcutaneous Nerve Stimulation (TENS)
- Scrambler therapy
- Spinal cord stimulation
TENs

- Electrodes placed with intention to treat most symptomatic CIPN area
- A small battery operated unit with 2-4 leads applied to skin via sticky attachment pads.
- Available for patients to use at home, following some simple instructions.

Scrambler Therapy

- Scrambler Therapy:
  - Electrodes placed with intention to treat most symptomatic CIPN area
  - Initially placed in the pathway of nerves innervating areas of pain, tingling, and/or numbness, but not directly on symptomatic areas of skin.

Scrambler Therapy & TENs: Clinical Data

• Loprinzi, C. et al.: Randomized, Controlled Phase II Pilot Trial:
  – 50 patients accrued, 25 to each of the 2 study arms; 46 patients were evaluable.
  – At least 3 months since chemotherapy cessation
  – Moderate, chronic CIPN symptoms at baseline
  – Randomly assigned to receive scrambler therapy or trans-electrical nerve stimulation (TENs) for 2 weeks
  – Patient reported outcomes
  – Treatments were given for 30 minutes.
  – Treatments scheduled to be given for 10 consecutive weekdays.

Scrambler Therapy & TENs: Clinical Data

- Loprinzi, C. et al.: Results

Scrambler Therapy & TENs: Clinical Data

• Loprinzi, C. et al.: Results

Scrambler Therapy & TENs: Clinical Data

- Loprinzi, C. et al.: Results

Scrambler Therapy & TENs: Clinical Data

- Loprinzi, C. et al.: Results Summary
  - Twice as many Scrambler-treated patients had at least a 50% documented improvement during the 2 treatment weeks from their baseline pain, tingling, and numbness scores in comparison to TENS-treated patients.
  - Global Impression of Change scores for “neuropathy symptoms”, pain, and quality of life were similarly improved during the treatment weeks.
  - Scrambler group more likely than TENS group to recommend their treatment to others, both during the 2 week treatment period and the 8 week follow-up period (P<0.0001).

Spinal Cord Stimulation

- Minimally invasive surgery
- Stimulator leads can be placed in many different regions
  - Most commonly in the epidural space to modulate the dorsal column of the spinal cord

- Modulates many different chemicals that work on pain
  - Increases GABA (helps to inhibit pain signals in the spinal cord)
  - Increases glycine
  - Decreases substance P

Neurostimulatory: Future Directions

- Evaluate optimal schedule for maintenance (scrambler)
- More data on spinal cord stimulation for painful CIPN needed
- Funding and availability of services
- Additional studies are needed to identify patients most likely to benefit from each type of neuro stimulatory approach

Outline

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• Future Strategies
Future Strategies

• Prior to treatment with neurotoxic chemo
  – Evaluate risk (A CIPN Risk Calculator taking into account clinical and biological predictors)
  – Evaluate Function including balance and gait and mobility
Future Strategies

- During neurotoxic chemotherapy
  - Patient reported outcomes
  - Dose modifications if symptoms worsening
  - Functional assessment longitudinally
  - Optimize reversible risk factors (diabetic control, physical activity levels)
  - Early referral to cancer rehab services if symptom burden increasing
Future strategies

- Post neurotoxic chemotherapy
  - follow symptoms which can linger for years
  - Cancer rehabilitation
  - Exercise and balance training
  - Use of additional modalities for individualized symptom management
Creating a cancer-free world. One person, one discovery at a time.
Thank you.

Questions?
Acupuncture: Mechanism

• Exact mechanism is under study
• May accelerate nerve regeneration
  – A positive correlation between the improvement in symptoms and nerve conduction function has been observed
• May affect inflammatory cytokines, neurotransmitters, or neurohormones.
  – Present study did not observe significant changes in these during the 10 weeks of acupuncture treatments.
  – Such changes may be difficult to detect in the MM study population
Scrambler Therapy & TENs: Mechanism

• Scrambler Therapy:
  – Cutaneous neuro-stimulatory therapy
  – Exchanges endogenous pain information with synthetic “non-pain” / “normal-self” electrical signals
    • Signals hypothesized to move through peripheral afferent somatosensory C fibers to the brain, innervating the region of pain.

• TENs:
  – Cutaneous neuro-stimulatory therapy
  – Electrical current pulse along the intact surface of the skin to activate nerves below.
  – Increased analgesia occurs when a strong, non-painful electrical paraesthesia beneath the electrodes is achieved