Chemo Brain and Fatigue

Chemotherapy Related Cognitive Impairment
Chemotherapy Related Fatigue

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Chemotherapy Related Cognitive Changes

- Attention
- Concentration
- Learning
- Memory
- Information processing
- Language
- Visuospatial skill
Scope of the Issue

• CRCI has been described since the 1970s
• Poorly understood
• Most of the data comes from breast cancer literature
  • 94% of BCS reported significant PCI 1 year following completion of chemotherapy
• 69% of OC survivors reported cognitive decline
• Even minimal impairment can profoundly impact QOL
  • As OS improves, attention to all aspects of QOL become more important
Description of the Experience

• “Walking into a room and forgetting what I was doing”
• Repeating themselves
• Misplacing keys and cell phones
• Names and phone numbers
• Trouble with word finding
• Repeating themselves
• Inability to multitask
• Reading comprehension and staying absorbed in a book
• Tasks taking longer
• Repeating themselves
• Feeling “foggy” and “spacy”
Impact of the Experience

- Depression, anxiety, frustration and embarrassment
- Family tension
- Withdrawing from social activities
- Job security
  - Difficulty returning to work when treatment is done
- Cognitive decline exacerbated by fatigue and stress
Timing of Cognitive Issues

- Wide range
- Sometimes no symptoms until chemotherapy completed
- Many symptoms after 1-2 cycles of chemotherapy
- Some noted improvement between cycles
- Some noted improvement 6-12 months following treatment
  - Some noted no improvement more than a year after chemotherapy
Direct effect of chemotherapy on CNS

- MTX and 5-FU cause progressive damage to myelin
- Minimal data on carboplatin and paclitaxel
  - One study of 28 Ov CA patients showed no EEG changes after 6 cycles of treatment
  - Reduced EEG processing speed 4 years following platinum in breast cancer patients
- Difficult to pinpoint specific chemotherapy agents
Indirect effects of chemotherapy on CNS

• Certain chemotherapeutics cause increased inflammation
  • Cytokine activation linked to:
    • Fatigue, sleep issues, poor concentration
    • Paclitaxel and docetaxel linked to increased levels of IL-6, 8, 10
• Increased free radical formation leads to neuron death
  • Especially in Adriamycin (Doxil)
    • Co-administration with anti-oxidants reversed these effects in mice
Non-treatment Causes

- Studies have shown cognitive decline before initiation of therapy
- Pain, fatigue and anemia
  - All have been shown to result in cognitive decline
- Hormone regulation
  - Increased glucocorticoid levels associated with cognitive decline
    - Dexamethasone for Taxol
  - Estrogen deficiency
    - Breast cancer patients who underwent both chemo and hormonal therapy showed the most deterioration and persistent decline
Official Diagnosis

• Difference in self-reported versus objectively measured
  • Some studies show up to 90% of patients exhibit cognitive decline
  • Some studies show no decline by objective measures
    • Prospective study in OC patients using carbo/taxol showed no decline
• 17 neuropsychological tests used to assess cognitive function
  • Heterogeneous group makes data interpretation difficult
• Imaging
  • Reduction in brain volume on MRI following chemotherapy in breast cancer
  • Lower resting metabolism on PET imaging of the brain following chemo
Patient Desires

- Information about possible cognitive decline BEFORE treatment starts
- Information to be shared with family, co-workers and friends
- Acknowledgement of the existence of cognitive decline
Coping Strategies

- Minimal quality research
- Needing to write things down
- Keep items in consistent locations
- Appropriate amounts of rest/sleep
- Structure and organize daily routine
- Relaxation techniques
- Meditation
- Exercise
- Crossword puzzles
Pharmacologic Interventions

• Erythropoietin (EPO)
  • 7 studies done – 3 with significant improvement
  • EPO no longer widely used due to significant risks

• Psychostimulants (Dexmethylphenidate and methylphenidate)
  • 8 published studies – mixed results
  • Minimal improvement in attention, memory

• Donepezil (cholinesterase inhibitor)
  • Two published trials – mixed results
Non-pharmacological Interventions

• Traditional Chinese Medicine
  • RCT of 81 Ov CA patients undergoing chemotherapy (carbo/taxol)
    • TCM consisted of herbs (?)
    • No difference in QOL noted and no difference in cognitive function
  • RCT of Medical Qigong showed improvement in cognition (all cancers)
    • 90 minutes/week for 10 months
    • Increased perceived cognition
  • RCT of Ginko biloba showed no improvement in cognition (all cancers)
Alternative Approaches

• Nature walks (breast cancer data)
  • 120 minutes/week of exposure to nature → improved attention/focus

• Exercise
  • Extensive research showing improvement in cognition
  • Tai Chi
    • 1 hour/week for 10 weeks
    • Improved perceived cognition but minimal objective response

• Cognitive Behavioral Therapy
  • Programs to improve/restore mental function
  • 4 large studies – 3 showed significant improvement in cognitive function

• Fruits and vegetables
  • CRC patients showed improved cognitive function
Cancer Related Fatigue

- Distressing, persistent, subjective sense of physical, emotional or cognitive tiredness/exhaustion related to cancer or therapy
  - Not proportional to recent activity
  - Significantly interferes with normal functioning
  - Not relieved by rest
Causes of Cancer Related Fatigue

• Progressive tumor growth
  • Metastatic disease
• Cancer therapy
  • Chemotherapy, surgery, RT
• Anemia
• Pain
• Emotional distress/depression
• Sleep disturbances
• Poor nutrition
• Medical co-morbidities
Prevalence of CRF

• Majority of patients undergoing treatment experience CRF
  • 75-90% of all patients
• 30% note persistent fatigue years following therapy
• Thought to be underreported
  • ASCO and NCCN recommend regular screening during treatment and surveillance/survivorship
• Most cases are mild-moderate
  • Recommend energy conserving activities
Severe CRF

• Focused history and evaluation
  • Anemia, metabolic disorders, endocrine issues, cardiac/pulmonary
  • Substance abuse, depression, sleep disturbance

• Non-pharmacologic interventions
  • CBT
  • Moderate aerobic exercise 150 min/week and strength training
    • Less fatigue/emotional distress, better sleep and QOL
  • Relaxation/stress reduction techniques, yoga
Pharmacologic Interventions

- **Psychostimulants**
  - Methylphenidate/dexmethylphenidate
    - Only 2 of 8 RCTs showed an improvement in fatigue scores
    - SSRI – only seem to benefit when fatigue accompanied by depression
- **Vitamins** – not effective
- **Ginseng** – beneficial while on treatment
  - Potential interaction with certain chemotherapies
Conclusions

• Cognitive Changes on Chemotherapy
  • It’s real!
  • Hard to officially diagnose but it is common
  • Multifactorial
  • Medication has mixed results
  • Exercise, mind-body techniques, CBT all seem effective

• Chemotherapy-Related Fatigue
  • Very common with a wide range of severity
  • Rule out underlying medical causes
  • Multifactorial
  • Medication has mixed results
  • Exercise, mind-body techniques, CBT all seem effective