

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 (Dexmethamphetamine 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