Chemotherapy Induced Peripheral Neuropathy and Balance Control in Pediatric Cancer Survivors

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Background

•Major treatment advances in pediatric cancers over the past several decades have led to a 5-year survival rate of 85%[1]
- Enhanced multi-drug chemotherapy treatments

•Many peripherally-administered chemotherapies cause chemotherapy-induced peripheral neuropathy (CIPN)
- Over 90% of the pediatric cancer survivors have CIPN[2]
- Vincristine, etoposide, and platinum-containing agents have been shown to cause neurotoxicity as a result of the death of peripheral neurons

•Intrathecal (IT) chemotherapy impacts the central nervous system and may also lead to neurotoxicity and exacerbate CIPN

Chemotherapy Drug	Drug Class	Mechanism of Action
Vincristine (VCR)	Vinca alkaloid	Alters the assembly and disassembly of microtubules, ultimately blocking mitosis and leading to cell death[3]
Carboplatin (CARBO)	Platinum-containing agent	Platinum-DNA Inhibits replication and transcription of the cell leading to cell death[4]
Etoposide (ETOP)	Topoisomerase II inhibitor	Inhibits topoisomerase II causing breaks in the DNA affecting cells metabolism eventually leading to cell death[5]

Table 1: Chemotherapy mechanisms

Purpose

The purpose of this study was to see if vincristine combined with IT chemotherapy or vincristine combined with a secondary neurotoxic chemotherapy (platinum's or etoposide) led to a higher level of CIPN and balance impairments in survivors of pediatric cancers.

Designs and Methods

	Cases (N=10)	Controls (N=10)
Inclusion Criteria	-Age: 12-21 -6 months to 10 years post-cancer treatment -Able to ambulate 10 meters unassisted -Treated with a neurotoxic chemotherapy -Able to speak English	-Age: 12-21 -Able to ambulate 10 meters unassisted -Able to speak English
Exclusion Criteria	- Advised by a medical professional to not perform strenuous activity -History of CNS cancer or cancers affecting lower extremities such as osteosarcoma or Ewing sarcoma - History of neurological disorder other than CIPN affecting motor skills or sensation	-History of cancer - Advised by a medical professional to not perform strenuous activity - History of neurological disorder affecting motor skills or sensation - Current orthopedic problems

Table 2: Participant criteria

Tests and Measures
•Chart reviews for type and cumulative dose of chemotherapies
•Pediatric-modified Total Neuropathy Score (Ped-mTNS)- Neuropathy assessment
•Bertec Sensory organization test (SOT) (Assessment of the use of sensory systems in balance control)

Analysis
•Descriptive statistics: means, standard deviations
•Independent sample t-tests
•Pearson product correlation

Strengths and Limitations

Strengths: Age and Sex matched controls

Limitations: Low variability in racial demographics
Small sample size
Female overrepresentation in cases and controls

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Results

	Case (N=10)	Control (N=10)
Gender		
Male	3 30%	3 30%
Female	7 70%	7 70%
Raw BMI	24.48 ± 6.7	22.75 ± 4.3
Age	18.5 ± 3.2	18.2 ± 3.3
Race		
Caucasian	5 50%	9 90%
Korean	1 10%	-
Asian	2 20%	1 10%
Hispanic	1 10%	-
Palestinian	1 10%	-
Neuropathy Present	7 70%	2 20%
Neuropathy Score Avg.	9.1 ± 6.8	2.5 ± 1.9

Table 3: Demographics Information

	Case (N=10)
Chemotherapy Type	
Vincristine	9 90%
Carboplatin	2 20%
Etoposide	5 50%
IT Methotrexate	5 50%
IT Cytarabine	4 40%
Brentuximab Vedotin	2 20%
Bendamustine	1 10%

Table 4: Chemotherapy Information

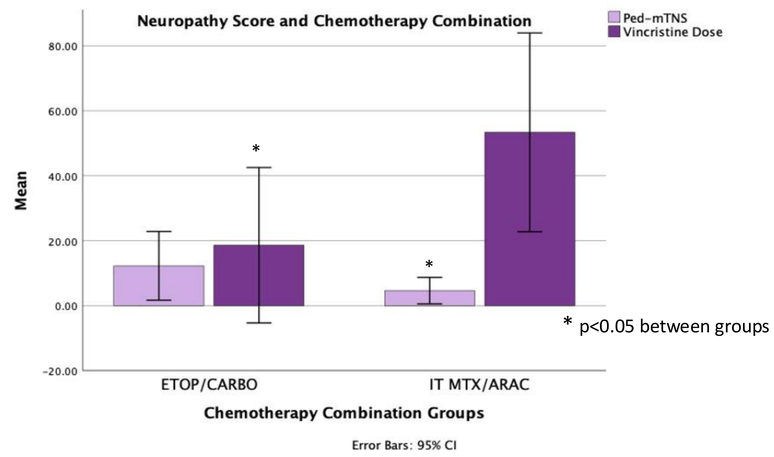

Figure 1: Ped-mTNS and vincristine dose comparison between chemotherapy groups

Vincristine combined with carboplatin and/or etoposide results in higher levels of CIPN (12.3 ± 3.3) than Vincristine with IT methotrexate and/or IT cytarabine (4.6 ± 6.7; p=0.050). The IT chemotherapy group received a higher cumulative vincristine amount (53.36mg/m2 ± 24.65) than the vincristine with carboplatin and/or etoposide group. (18.60mg/m2 ± 15.04; p= .018).

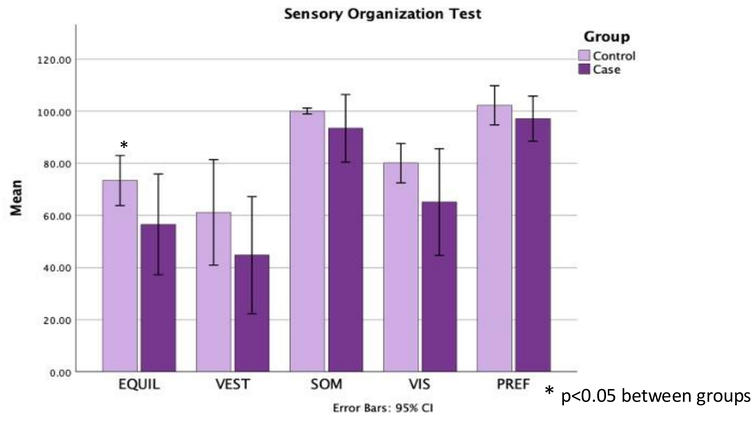

Figure 2: SOT score between pediatric cancer survivors and controls

Overall equilibrium score on the SOT was worse in cancer survivors (56.56 ± 27.00 vs. 73.40 ± 13.43, p = 0.050), yet the severity of the neuropathy was not associated with the balance outcomes (r = -0.287, p = 0.220).

No significant difference in SOT subscale scores was seen between chemotherapy treatment groups (p>0.05).

Conclusion and Next Steps

Ped-mTNS and Chemotherapy Groups
•Cancer survivors who received both vincristine and a secondary neurotoxic chemotherapy (platinum's and etoposide) compared to vincristine plus IT chemotherapy scored significantly higher on the Ped-mTNS indicating a worse CIPN
- Not due to higher cumulative dosage of vincristine

SOT Scores
•While balance control was worse in cancer survivors, the severity of neuropathy appeared to have no association with balance outcomes
•Both CIPN and balance need to be evaluated in pediatric cancer survivors.

What Needs to Come Next
•Further studies with larger sample sizes of both cases and controls
•Further research into a possible influence of two neurotoxic chemotherapies leading to higher level of CIPN
•Further research into the CNS to better understand balance outcomes in survivors

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