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School of Nursing

Standing on Pins and Needles?
Patterns and Severity of Vincristine-Induced Peripheral Neuropathy in Children with Acute Lymphoblastic Leukemia

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BACKGROUND & SIGNIFICANCE

Vincristine Induced Peripheral Neuropathy (VIPN) occurs in nearly all children receiving vincristine (VCR) for acute lymphoblastic leukemia.(ALL).[1,2] Symptoms include numbness, tingling, and pain in the hands & feet. Few studies have described VIPN severity, patterns, and variables associated with an increased risk for developing retractable symptoms. It is important to gain knowledge about VIPN patterns and severity because symptoms can be chronic and disabling in a highly curable patient population. Study findings may lead to future interventions to minimize VIPN-related life-long functional and quality of life impairments.

PURPOSE & AIMS

Purpose: To describe VIPN severity, clinical manifestations, and patterns when assessed over the first year post-diagnosis n children ages 1-18 with ALL.

The study aims were to:

1. Describe VIPN incidence, patterns, and severity.
2. Describe the relationship between dose density and VIPN.
3. Describe the predictors of more severe VIPN.

SAMPLE & SETTING

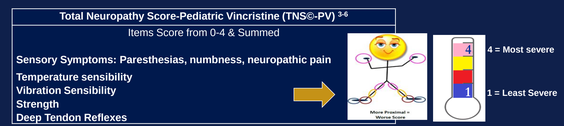
Eligibility Criteria: Newly diagnosed children > 1 and < 18 years old with ALL who would receive standardized VCR dosing

Sample/Setting: 128 newly diagnosed children receiving vincristine 1.5 mg/M2 (2mg maximum) per Children's Oncology Group treatment trials were recruited from four sites (Indiana University, University of Michigan, Vanderbilt University, Children's National)

METHODS

Design: Longitudinal, prospective study

Measurement: VIPN and pain were assessed before each VCR dose over the first year of treatment using the TNS©-PV.



DATA ANALYSES

Data were analyzed using descriptive statistics (frequencies, means, and standard deviations), correlations, paired t-tests, and cluster analysis. Vincristine dose density curves were calculated based on the kernel density function.

RESULTS

Demographics: VIPN and neuropathic pain assessments (N = 1961) were performed on equal numbers of males and females. Most were Caucasian (87.7%) and non-Hispanic (78.1%). The mean age was 6.16 (SD 4.96) years (range 1-18).

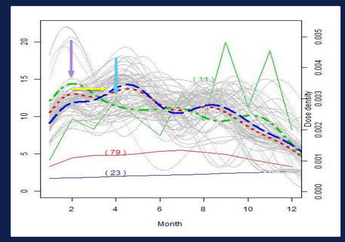
Aim 1: Describe VIPN incidence, patterns, and severity.

In the first year following diagnosis:

- 100% developed VIPN
- 100% developed painful VIPN

VIPN Signs and Symptoms				
	N	Mean	Std. Error	Range
Paresthesia	1324	0.11	0.02	0-4
Numbness	1323	0.09	0.02	0-4
Neuropathic Pain	1333	0.17	0.02	0-4
Temperature	1199	0.32	0.03	0-4
Vibration	1167	0.67	0.04	0-4
Strength	1327	0.52	0.03	0-4
Reflex	1352	1.63	0.05	0-4

TNS © Total Score



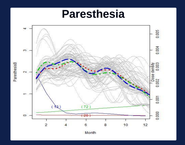
- Mean TNS©-PV individual item scores were generally low for most children.
- Reflexes were affected most (mean/SD = 1.63/0.05, range 0-4) and could be evaluated in nearly all (88.2%) children.
- TNS©-PV scores in some patients (green cluster) (*n* = 11) peaked 4 months from diagnosis, approximately 2 months after reaching the maximum vincristine dose density, illustrating a coasting effect.
- TNS©-PV scores for most children (blue and red clusters) (*n* = 102) peaked at month 6-7.

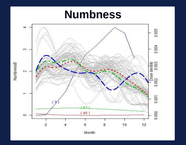
Graphs Legend

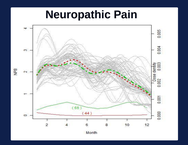
- Dose density peak (highest VCR treatment frequency)
- Coasting effect
- Symptoms peak
- Cluster 1 mean VIPN scores
- Cluster 2 mean VIPN scores
- Cluster 3 mean VIPN scores
- Cluster 1 mean dose density
- Cluster 2 mean dose density
- Cluster 3 mean dose density
- Individual dose density

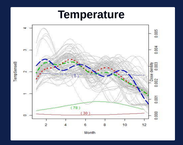
Aim 2: Describe the relationship between dose density and VIPN.
Aim 3: Describe the predictors of more severe VIPN.

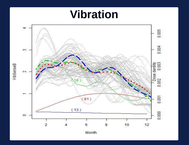
VIPN Signs & Symptoms

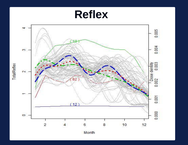


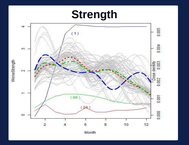












- TNS©-PV total (see Aim 1 graph) and individual item scores did not significantly improve in months 8-12 despite decreasing vincristine dose density over time.
- TNS©-PV scores were positively associated with age (*p* = .0095) but not gender.
- Two to three distinct clusters emerged from the data revealing some children (*n* = 11) experienced severe VIPN unrelated to dose density.

CONCLUSIONS

All children developed VIPN and pain. Symptom severity was low in most cases. VIPN is most severe 4-7 months from the onset of ALL treatment, and did not improve despite children receiving less vincristine in months 8-12. Cluster analysis results suggest that some children are at more risk than others for developing severe VIPN. Further research is ongoing to identify a baseline clinical "signature" for identifying high-risk patients

LIMITATIONS

- Study findings cannot be generalized to neuropathy caused by other neurotoxic agents, or to non-leukemia populations.
- Interpretation of dose density and cluster analysis are qualitative.
- Early peak strength may be due to steroid myopathy

IMPLICATIONS FOR PRACTICE & RESEARCH

Practice:

- The study findings:
  - May be used to educate patients and families of what to expect from vincristine treatment for ALL.
  - May lead to more effective strategies to treat and/or prevent VIPN in a highly curable patient population.

Research:

- Further research is needed to:
  - Discover additional predictive variables , such as genetic polymorphisms, that will identify high risk patients.
  - Inform targeted treatment and preventative approaches for high risk patients.

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