

Pediatric Chemotherapy: Effect on Peripheral Neuropathy

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Abstract

A high-quality synthesis of the empirical evidenceregarding chemotherapy-induced peripheral neuropathy (CIPN) characteristics and patterns described in studies of children who received neurotoxic chemotherapy to treat cancer and caucasian race is a risk factor and, contrary to prior thinking, cumulative chemotherapy dosage alone does not predict CIPN severity. The influence of other risk factors is less clear, and studies to date have not explored potential interactions among race, genetics, age, sex, drug metabolism, and nutritional status, among other factors.

Keywords: Pediatric; Chemotherapy; Peripheral neuropathy

Introduction

Chemotherapy-induced peripheral neuropathy (CIPN) is found more frequently in children with acute lymphoblastic leukemia (ALL). Neurological classification can be grouped into one of the three working divisions of the peripheral nervous system, sensory, motor and autonomic. Most among the chemotherapeutic agents used in ALL is vincristine which has been associated with neuropathy in these children. This can be of neuropathy and can be transient but also leave permanent sequels that decrease patient's quality of life. Advances in treatment have resulted in a growing number of adult survivors of pediatric cancers; however, survival comes at a price, given that cancer treatments can frequently cause long-term and debilitating comorbidity. Chemotherapy-induced peripheral neuropathy (CIPN) is a common side effect of neurotoxic drugs treatment. Numbness, tingling, and neuropathic pain in the both upper and lower extremities, weakness, loss of ankle dorsiflexion range of motion (foot drop), and impaired balance are the most common CIPN manifestations. CIPN negatively influence the children's working capacity and engagement in physical activities. Although duloxetine is only the effective intervention to mitigate painful oxaliplatin-induced CIPN in adults, reduction or discontinuation of the offending neurotoxic agent is the only known approach to ameliorate moderate to severe CIPN symptoms in children. However, decreasing che-

motherapy dose will compromise patients' survival outcomes.

Discussion

The characteristics and variations of CIPN vary widely depending on the chemotherapy drug/dose/schedule used and predisposing risk factors (e.g., diabetes, inherited neuropathy). Through comparisons of CIPN characteristics and patterns resulting from various neurotoxic drugs treatment we can gain insight in to how to look over high-risk patients, and treat established CIPN, and prevent the conditions of altogether. The purpose of this review is to provide a systematic synthesis of the empirical evidence about CIPN characteristics—defined as the incidence and severity of numbness, tingling, pain, motor deficits, and autonomic manifestations—and patterns (i.e., onset, duration, and predictors) described in studies of children who received any type of neurotoxic chemotherapy. A discussion of genetic predictors of CIPN is beyond the scope of the article, and thus not addressed here. The dramatic rise in the number of childhood cancer survivors over the last 60years has made monitoring and minimising long term side. Chemotherapy induced peripheral neuropathy (CIPN) has been described with more commonly used chemotherapy agents. This research work provides a critical overview of pediatric CIPN, its incidence, clinical manifestations, late effects, and recent. Though acute symptoms of neuropathy diminish quickly after dose changing or conclusion of treatment with vincristine, it is accurate that underlying effects are prolonged into adolescent years and adulthood in pediatric cancer survivors. Hoffman et al 21 studies number of aspects of physical performance among adolescent All survivors with an average time of 9.3 years since final dose and compared testing results to their siblings. They found that survivors of childhood ALL treated with chemotherapeutic agents including Vincristine, had lower scores than siblings tested with the 6-minute walk test, Timed Up and Go, and strength measured with dynamometry. This was true even in siblings who maintained same active lifestyles. Deficits in physical performance continue to persist even through adult years. Ness et al list slowed motornerve NCV, absent deep tendon reflexes, limited ankle range of motion, and distal muscle weakness among the primary impairments seen in

survivors of ALL with an average of 28 years past their final dose and mean age of 35.6 years.

Aspects of balance, mobility, ankle strength and range, and sensation in a cohort of adult ALL survivors treated previously with various chemotherapeutic agents including Vincristine. Frequency distribution of impairments to note include reduced ankle dorsiflexion AROM of lesser than 5 degrees in 33.5%, ankle plantar flexion weakness in 24.6%, and ankle dorsiflexion weakness in 16.9%. An association was made between those participants having had a additive vincristine dose of >39 mg/m² and increased likelihood of 1.5 times greater to have reduced dorsiflexion AROM. Furthermore, the authors further investigated the impact these impairments had on participants ultimate physical performance 10 attributes including walking efficiency as tested using the 6-minute walk test. They found that participants with reduced dorsiflexion AROM subsequently had lower scores on the 6-minute walk test compare to the predicted values for healthy individuals with similar age, weight, height, and sex. These authors suggest that those participants who received high cumulative doses of Vincristine and subsequent neuropathic impairments were limited in physical performance measures compared to their healthy subjects. Most research about this topic centers around survivors of ALL, yet as Harman et al²² mention, Vincristine is the main chemotherapeutic substance used to treat a different pediatric cancers such as non-Hodgkin's Lymphoma, Wilms tumor, and with malignant mesenchymal tumors. Hartman et al²² seek to address this

deficit in research with their study concerning muscle weakness and ROM deficits in survivors of these cancers an average of 3.3 years after their final dose of vincristine. They found that the average dorsiflexion ROM and strength as measured with dynamometry in survivors was significantly less than those of healthy controls. Passive dorsiflexion ROM deficits were found in 32% of cancer survivors compared to only 14% of control. Since 5 degree is considered the necessary range for normal gait, the authors estimate that those survivors with less than 5 degrees, combined with subsequent shortening of the gastrocnemius, will limit all physical performance. Disorder of peripheral nerves are frequent complications of chemotherapy and certain other drug therapies. As more and more effective therapies for cancer are across number of patients who are living longer, peripheral neuropathy complications of chemotherapy is increasing in prevalence. Chemotherapy can cause loss in peripheral sensory and motor nerves and cause patients to present.

Conclusion

While these studies guide suggestions for current clinical practice, further systematic research with development of strategies for amelioration and prevention of CIPN is necessary. Standardised assessment protocols and objective outcomes measures of CIPN applicable to patients of different ages are critical to enabling the development of novel treatments and facilitation of future clinical trials and treatment individualisation.