RESEARCH BRIEF

Exploring Daily Salivary Cortisol Patterns as Biomarkers of Chronic Chemotherapy-Induced Peripheral Neuropathy Pain

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OBJECTIVES: Little is known about the biologic mechanisms of chronic chemotherapy-induced peripheral neuropathy (CIPN) pain. The purpose of this secondary analysis was to explore salivary cortisol patterns among cancer survivors with chronic CIPN pain to provide preliminary data regarding the role of hypothalamic-pituitary-adrenal axis dysregulation in the pathophysiology of this condition.

SAMPLE & SETTING: 13 cancer survivors with chronic CIPN pain recruited from the breast, gastrointestinal, and gynecologic cancer centers at Dana-Farber Cancer Institute in Boston, Massachusetts.

METHODS & VARIABLES: Salivary cortisol was collected on awakening, 30 minutes after awakening, and before going to bed on two consecutive days. Cortisol awakening response and diurnal cortisol slope were calculated by averaging results across two days.

RESULTS: Cortisol was available from 13 participants. The median cortisol awakening response was –0.03 mcg/dl, and the average diurnal cortisol slope was –0.24 mcg/dl.

IMPLICATIONS FOR NURSING: Mechanism-based treatments are needed for cancer survivors with chronic CIPN pain. Nurse scientists may use study results to explore stress-related mechanisms of chronic CIPN pain.

KEYWORDS chemotherapy-induced peripheral neuropathy; biomarker; cancer survivors; cortisol; HPA axis

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Chemotherapy-induced peripheral neuropathy (CIPN) is a disabling side effect of neurotoxic chemotherapy that causes neuropathic symptoms (e.g., numbness, tingling, shooting/burning pain) in the upper and lower extremities (Winters-Stone et al., 2017). Duloxetine (60 mg per day) is the only recommended drug for CIPN pain, and the strength of recommendation for its use is moderate (Loprinzi et al., 2020). Little is known about the mechanisms of underlying chronic CIPN pain, making it difficult to develop mechanism-based treatments for this condition.

Although neurotoxic chemotherapy agents have varying antineoplastic mechanisms of action, all are believed to directly or indirectly invoke a dying-back axonopathy that is responsible for the development of CIPN (Fukuda et al., 2017). Chronic CIPN results from permanent changes in the structure and functioning of the central nervous system and is therefore defined as neuropathic pain (Baron et al., 2010). One potential aspect of chronic CIPN development is dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, which is a primary regulator of the stress response (Eller-Smith et al., 2018). In healthy adults, HPA axis activation results in the release of cortisol to decrease peripheral inflammation (Eller-Smith et al., 2018). HPA axis activation ceases when cortisol binds to receptors in the hippocampus (Eller-Smith et al., 2018). However, in response to chronic stress, such as peripheral nerve injury, processes associated with HPA axis dysregulation (e.g., amygdala activation, increased corticotropin releasing factor) are initiated and result in cortisol dysfunction (Eller-Smith et al., 2018). In the absence of functioning cortisol, peripheral nerve injury results in unchecked peripheral inflammation and increased sensitization