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Chemotherapy-Induced Peripheral Neuropathy in Multiple Myeloma Patients

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Abstract
This study aimed to evaluate the symptoms of chemotherapy-induced peripheral neuropathy (CIPN) and its impact on health-related quality of life (HRQOL) in multiple myeloma (MM) patients. A cross-sectional survey was conducted among MM patients at a tertiary care hospital, utilizing the European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire for CIPN scale (QLQ-CIPN20) and the EORTC multiple myelo ma module (QLQ-MY20). Descriptive statistics were used for data presentation. 26 patients participated, with 61.5% being male. The average age was 64.34±8.49 years. CIPN symptoms included tingling, numbness and difficulty in walking. HRQOL challenges encompassed bone pain, back pain, feeling ill, hair loss and concerns about health and mortality. MM patients experience CIPN symptoms, impacting their HRQOL. Incorporating CIPN assessments as patient-reported outcomes is crucial in routine clinical practice.

INTRODUCTION

Progress in cancer therapy has brought about a gradual shift in long-term treatment effects, patient-reported outcomes and overall patient experience[1]. One prevalent long-term neurological side effect is chemotherapy-induced peripheral neuropathy (CIPN), resulting from chemotherapy treatment[2]. CIPN is associated with debilitating symptoms that significantly impact a patient's quality of life (QoL)[3]. The reported incidence of CIPN varies widely, ranging from 30-70%, with this variability attributed to diverse assessment methods employed[4,5]. The occurrence of CIPN is influenced by factors such as the type and dosage of chemotherapy[6,7] and its prevalence diminishes over time since the initiation of chemotherapy: 68% of patients experience it in the first month, 60% at 3 months and 30% at 6 months[8].

The manifestation of chemotherapy-induced peripheral neuropathy (CIPN) symptoms is contingent on the specific chemotherapy employed. These symptoms typically impact both upper and lower limbs in a distinctive "stocking-and-glove" pattern, extending to the orofacial region[6,10-12]. The onset of symptoms is gradual, commencing in the lower limbs and progressing to the upper limbs[2]. Sensory manifestations, such as pain, dysesthesia, numbness, and tingling in the hands and feet, are more prevalent and prominent compared to autonomic symptoms like constipation, urinary retention and erectile dysfunction[6,8,10,12]. Clinical examination often reveals impaired perception of touch, vibration and proprioception[1]. These symptoms can be debilitating, significantly affecting the quality of life (QoL)[2,13]. Various tools have been documented in the literature for CIPN assessment, including the 20-item scale of the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire for CIPN (QLQ-CIPN20), acknowledged for its reliability and internal validity (Cronbach's α: 0.88)[14,15,16].

MATERIAL AND METHODS

In November 2021, a cross-sectional survey was conducted in a tertiary care hospital to evaluate chemotherapy-induced peripheral neuropathy (CIPN) and health-related quality of life (HRQOL) among patients diagnosed with multiple myeloma (MM). The study received ethical approval from the Institutional Review Board (IRB). Patients aged 18 years and above, both male and female, diagnosed with multiple myeloma (MM) since 2017, initiated on chemotherapeutic agents and currently attending the hematology clinics/ward at a tertiary care hospital, were invited to participate in the study using a convenient sampling method. Enrollment in the study was contingent on patients signing written informed consent.

Chemotherapy-induced peripheral neuropathy (CIPN) was evaluated utilizing the Arabic version of the self-reported tool, EORTC QLQ-CIPN20, which comprises 20 items categorized into three subscales: sensory (nine items), motor (eight items) and autonomic symptoms (three items). Participants rated items on a Likert scale ranging from 1 (not at all) to 4 (very much). The final scores were transformed linearly to a scale of 0-100, where a higher score indicated a greater symptom burden[14]. Health-related quality of life (HRQOL) was assessed using EORTC Multiple Myeloma Module, QLQ-MY20. This module includes two subscales: a functional domain (4 items) and a symptoms domain (16 items). Scores were also linearly transformed to a 0-100 scale, with a higher score reflecting an improved quality of life.

RESULTS AND DISCUSSIONS

A total of 26 patients participated in the study, comprising 16 men (61.5%) and 10 women (39.5%), with an average age of 64.34±8.49 years. The mean duration of multiple myeloma (MM) was 3.08±2.68 years. Approximately 87% of patients underwent active chemotherapy, with bortezomib-cyclophosphamide-dexamethasone being the most common regimen. Among the patients, 47% received thalidomide and 14% were exposed to more than one neurotoxic agent. Additionally, 22% of patients underwent radiotherapy and few of them received autologous stem cell transplantation (4 patients). Regarding comorbidities, 54% had diabetes mellitus, 27% had hypertension and 9% had ischemic heart disease. Five patients (9.0%) had a history of prior malignancy and 10% had myelodysplastic syndrome. Treatment response data were available for 14 patients, with 53% experiencing relapse, 28% achieving partial response and 17% achieving complete response.

Among the 26 participants, 37.8% reported tingling in fingers/hands and 23% in toes/feet on the sensory scale. Numbness was noted by 49% in fingers/hands and 57% in toes/feet. Shooting or burning pain was reported by 14% in fingers/hands and 26% in toes/feet. Trouble standing or walking was reported by 43% and 13.7% experienced hearing difficulties. Only 9% reported difficulty distinguishing between hot and cold water. On the motor scale, 49.78% reported trouble walking, while 54.3% faced difficulty in climbing stairs and standing up from a chair. Regarding driving, 21% of the participants who drove reported "quite a bit" or "very much" trouble using pedals. On the autonomic scale, 27% reported orthostatic hypotension, 44.6% had blurred vision and 21.5% reported erectile dysfunction. However, mean scores on CIPN subscales did not significantly differ between patients with and without diabetes for

sensory (p = 0.29), motor (p = 0.723), or autonomic (p = 0.541) scales.

Peripheral neuropathy is the most prevalent chemotherapy side effect in multiple myeloma (MM) patients. However, these symptoms may not be exclusively related to chemotherapy, as age and comorbidities like diabetes can contribute. The EORTC QLQ CIPN20 proves to be a valid tool for identifying CIPN in MM patients, with participants taking an average of 5 minutes to complete the Arabic questionnaire, making it feasible for routine care.

CIPN linked to bortezomib and thalidomide is reversible, with 80% of patients becoming asymptomatic upon bortezomib discontinuation. However, symptoms may persist after chemotherapy cessation and a guaranteed cure is not assured. Monitoring CIPN symptoms over time is crucial for chemotherapy dose adjustments.

Comparing these results with other studies poses challenges due to variations in assessment tools and symptom frequencies. While sensory symptoms reported in this study occur less frequently than in some studies, erectile dysfunction is more common. CIPN differentiation from other neuropathies, such as diabetic and paraneoplastic neuropathies, is intricate. In this study, 66.4% of participants reported at least one bothersome symptom significantly impacting daily life activities.

Limitations of this study include the inability to capture the baseline disease status of participants, leading to potential overlap with preexisting peripheral neuropathy symptoms from conditions like diabetes. The absence of a control group makes it challenging to compare observed frequencies with those in the broader population. Despite including all MM patients diagnosed over 5 years, the sample size may not be sufficient to conclusively attribute peripheral neuropathy to a specific chemotherapy.

CONCLUSION

Chemotherapy-Induced Peripheral Neuropathy (CIPN) is closely linked to a decline in Health-Related Quality of Life (HRQOL) among affected individuals. The severity of symptoms warrants careful consideration for chemotherapy dose modification or discontinuation. Recognizing CIPN as a patient-reported outcome is essential in routine clinical practice, emphasizing the importance of incorporating patient experiences and subjective assessments into treatment decisions. Monitoring and addressing CIPN through patient-reported outcomes contribute to a more comprehensive and patient-centered approach in managing cancer treatment side effects. This approach ensures that the impact of CIPN on an individual's daily life and well-being is taken into account when determining the course of chemotherapy, optimizing both treatment efficacy and the patient's overall quality of life.

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