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The development of an EORTC quality of life questionnaire to assess chemotherapy-induced peripheral neuropathy: The QLQ-CIPN20

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Abstract

Chemotherapy-induced peripheral neuropathy (CIPN) is a common phenomenon, often resulting in serious limitations in daily functioning and comprosised quality of life. Currently available toxicity grading systems typically use a combination of clinical and paraclinical parameters and relies on the judgment of clinicians and/or nurses. However, because many of the symptoms of CIPN are subjective in nature, it is only logical that an assessment of CIPN be based, at least in part, on patient self-report data. We report on the development of a patient self-report questionnaire, the CIPN20, intended to supplement the core quality of life questionnaire of the European Organization for Research and Treatment of Cancer (EORTC). Following EORTC guidelines, relevant CIPN-related issues were identified from a literature survey and interviews with health professionals ($n = 15$) and patients ($n = 112$). The resulting 20-item questionnaire was pre-tested in three languages and four countries and is currently being examined in a large, international clinical trial. The EORTC CIPN20 should provide valuable information on CIPN-related symptoms and functional limitations of patients exposed to potentially neurotoxic chemotherapeutic and/or neuroprotective agents.

Keywords: Chemotherapy; Peripheral neuropathy; Quality of life questionnaire; EORTC; QLQ-CIPN20

1. Introduction

Peripheral neuropathy can be defined as a derangement in structure and function of peripheral motor, sensory and autonomic neurons causing peripheral neuropathic signs and symptoms. Chemotherapy-induced peripheral neuropathy (CIPN) is a major, potentially dose-limiting side effect of several chemotherapeutic agents including platinum analogs, vinca alkaloids and taxanes. The incidence of CIPN may be as high as 100% in treated patients, depending on dose and dose-intensity of the chemotherapy regime. The neurotoxic side effects may be very long lasting and its treatment

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is usually difficult. Neuroprotective agents are currently being investigated to prevent or ameliorate CIPN.

Chemotherapy-induced peripheral neuropathy may seriously compromise patients' quality of life (QL) [1,2]. Therefore, it is important to be able to assess CIPN in a valid and reliable manner, both in clinical trials of new chemotherapeutic agents and in clinical practice, where the treatment is known or suspected to induce CIPN [3]. The two most widely used cancer-specific QL questionnaires are the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 and the Functional Assessment of Cancer Therapy (FACT-G) [4,5]. Both of these questionnaires are designed to assess a core set of QL issues and are intended to be supplemented by additional condition- or treatment-specific modules or subscales. Recently, a paclitaxel-induced peripheral neurotoxicity module was added to the FACT measurement system, comprising eleven neurotoxicity and five paclitaxel-related items [6,7]. The EORTC measurement system does not yet have a CIPN module, although several of the existing EORTC questionnaires include a few items pertaining to CIPN (e.g., pain, paresthesias). The primary objective of the current project was to develop a questionnaire module on CIPN to supplement the EORTC QLQ-C30.

2. Patients and methods

To ensure scientific rigor and quality, the EORTC Quality of Life Group has generated detailed guidelines for developing QL questionnaire modules [8]. The developmental process comprising four phases is shown in Table 1. This process was supervised by the EORTC QL Group. In this manuscript we describe the first three phases of the development of the CIPN module, the QLQ-CIPN20.

Table 1
Phases of development of the EORTC QLQ-CIPN20

Phase I – generation of quality of life issues
Literature search
Semi-structured interviews with health care professionals and patients
Selection of issues
This yields a list of potentially relevant QL items
Phase II – operationalisation
Construction of a provisional questionnaire
Items worded to be compatible with the QLQ-C30 format
Forward and backward translation
Phase III – pre-testing
Patients complete the questionnaire and undergo a "debriefing" interview
Data are analysed according to preset criteria (e.g. response prevalence and variance)
Formal report submitted to the EORTC QL group
Approval by the EORTC QL group
Phase IV – international field testing
Extensive evaluation of reliability, validity and responsiveness to change over time

3. Results

3.1. Phase I literature search

A Medline literature search was conducted, using the following keywords: chemotherapy and neuropathy, quality of life, health status or performance, questionnaire and peripheral neuropathy. In almost all of the oncology literature identified with this search, CIPN was assessed by means of standardised, physician-rated toxicity scales such as that of the World Health Organization and the Common Toxicity Criteria. Other studies employed single-institution classification systems that also relied on physicians' ratings [9–13].

In the neurology literature, several scales for assessing neuropathic signs and symptoms have been developed, including the Neuropathic Symptoms Score, the extensive Neuropathy Symptom Profile and the Neurological Disability Score [14–16]. These physician-based scales have been used primarily in clinical studies of diabetic neuropathy and most assessed the prevalence rather than the severity of symptoms. The Total Neuropathy Scale is a composite physician-based score using a combination of clinical features and neurophysiological parameters, formally validated for patients with diabetes mellitus but also used in small series of patients with cancer. Recently, a comparison was performed between the Total Neuropathy Scale and common oncological grading scales, which showed moderate correlations [17]. However, QL issues are not addressed in this approach. A patient-based diabetes symptom checklist is also available, but it contains only a limited number of neuropathy-related items [18].

3.2. Phase I selection of key issues

The literature review yielded 29 issues related to peripheral neuropathy. This list of issues was initially reviewed for completeness, relevance and importance by nine health care professional from the Netherlands and included: two medical oncologists, two hematologists, four neuro-oncologists and an oncology research nurse. Subsequently, two French neurologists, one Belgian neurologist, one British neurologist and two British medical oncologists were also asked to review this list of issues. All 15 of these individuals also provided suggestions for additional issues that had not been identified by the literature review. On the basis of this structured exercise, a provisional questionnaire consisting of 33 items was constructed in the Dutch language and translated into English and French following the