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Impact of chemotherapy-induced nausea and vomiting on health-related quality of life and resource utilization: A systematic review

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ABSTRACT

Background: Chemotherapy-induced nausea and vomiting (CINV) is a particularly distressing event for oncology patients. This review aims at analyzing the impact of CINV on Health-Related Quality of Life (QoL) and on the use of healthcare resources.
Methods: A systematic search was conducted according to the PRISMA statement on MEDLINE, EMBASE and NHS EED.
Results: Sixty-seven studies were included in the final selection. Despite the availability of numerous treatment options, CINV was found to have a strong impact on HRQoL of patients. Direct costs are particularly affected, but this result could be due to scarcity of studies assessing indirect costs.
Conclusions: Evidence supports the notion that CINV continues to have a negative impact on HRQoL of patients, even for those receiving moderately emetic chemotherapy. Further studies need also to collect data on the cost of CINV, particularly indirect costs, to ensure that decisions on use of healthcare resources are better supported.

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1. Background

Nausea and vomiting represent a common side-effect of chemotherapy, potentially affecting 60–80% of oncology patients (ONS, 2014; de Boer-Dennert et al., 1997). Nausea is defined as the unpleasant feeling causing the desire to vomit, and can be accompanied by symptoms such as tachycardia, dizziness and weakness (Camp-Sorrell, 2005). Vomiting is defined as the contraction of the muscles of the abdomen and diaphragm that triggers the expulsion of stomach contents (Baker et al., 2005). Chemotherapy-induced nausea and vomiting, CINV, also referred to as emesis, is a particularly distressing event for oncology patients, both from a physical and psychological perspective; yet the perception of its burden is often not equal between patients and healthcare professionals, with 75% of the latter group underestimating CINV incidence and severity (Grunberg et al., 2004). Despite not being life-threatening, CINV can influence patients' willingness to continue chemotherapy, and thus impact survival outcomes (Hassan and Yusoff, 2010; Aapro, 1991).

A study conducted on 14 oncology centres in six countries has shown that more than 35% of patients has acute nausea and more than 10% develops acute vomiting. Overall, around 35% of patients experiences acute CINV and around 60% develops delayed CINV (Ihbe-Heffinger et al., 2004). Anticipatory vomiting occurs in around 1.5–2.3% of patients before cycles 2 and 3 of chemotherapy, while the incidence of anticipatory nausea is around 5–8% before cycles 1–3 (Chan et al., 2015). The factors affecting the incidence and severity of CINV are type of chemotherapy, form of administration and characteristics of individual patients (Institute, N.C. Nausea and Vomiting, 2014).

Individual risk factors include gender, age and control of prior chemotherapy (American Society of Clinical Oncology et al., 2006). In particular failure to treat CINV increases the probability for patients to incur in this side effect in later episodes (Hassan and Yusoff, 2010).

These epidemiological data show the clinical significance of CINV and become even more relevant when considering the impact of CINV on patients' quality of life (Cohen et al., 2007; Navari, 2013; Philip and George, 2014). CINV can affect patients' daily functioning, leisure activities and ability to eat and drink (Boccia, 2013). Emesis also entails more inpatient, outpatient and emergency room visits, resulting in heightened healthcare resource utilization and heightened costs of cancer treatment (Burke et al., 2011). However, such effects may be avoided or limited and, with the correct use of antiemetic treatments, nausea and vomiting can be reduced for up to 80% of patients undergoing chemotherapy (Philip and George, 2014; Jordan et al., 2014). Such therapies are based on the neurochemical control of vomiting and the receptors involved in vomiting regulation, such as serotonin (5-HT3) (Hornby, 2001).

Based on the major antiemetic guidelines (ASCO, MASCC/ESMO, NCCN), the choice of the prophylaxis depends on the level of emetogenic risk faced by patients. For example, based on MASCC guidelines, in patients undergoing highly emetogenic chemotherapy (HEC), 5HT3 receptor antagonists, RAs (first and second generation), corticosteroid and NK-1 RAs are recommended, in patients receiving moderately emetogenic chemotherapy (MEC) palonosetron and corticosteroids are recommended, while for low-risk patients other treatments such as dopamine receptor antagonists and cannabinoids are recommended (Boccia, 2013; MASCC, 2013). A study showed that, when caregivers were following the guidelines, approximately 60% of patients did not experience CINV, compared to 50% of patients in those cases when treatment regimens were inconsistent with MASCC guidelines (Aapro et al., 2012).

Despite the presence of several therapeutic options, there are still unmet needs related to CINV due to its impact on morbidity and quality of life of oncology patients (Decker et al., 2006). This review aims at analyzing two key issues. First, the impact of CINV on Health-Related Quality of Life (HRQoL) is investigated by retrieving studies that measured changes in quality of life for oncological adult patients due to emesis. Secondly, the effect of emesis on the use of healthcare resources and the additional costs that could be potentially saved if unmet needs were addressed by new antiemetic agents are analyzed.

2. Methods

2.1. Identification of studies

This review adopts the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement (Moher et al., 2010). A systematic search was conducted on MEDLINE, EMBASE and the National Health System Economic Evaluation Database (NHS EED). Reference lists of the most relevant retrieved articles were screened to find additional studies not identified through the database search. The search strategy was developed using the PICOS (Patient, Intervention, Comparator, Study) framework. The searching strategies used for economic studies were specific for EMBASE (McKinlay et al., 2006) and for MEDLINE (Sassi et al., 2002; Wilczynski et al., 2004), with a simplified version for NHS EED database. The search filter for HRQoL studies was an adapted filter developed by the NHS Center for Reviews and Dissemination (University of York). These search strings were complemented with a set of indexed and loose terms such as Emesis, CINV, quality of life, utilities, health measure (Fitzpatrick et al., 1998). Boolean operators "AND" and "OR" were used to combine terms, while "NOT" operator was not included following Cochrane indications. Date and place limits were not be set for this review. The search was conducted in December 2014. The search strategies, as well as the review protocol, are available upon request.

2.2. Selection of studies

The selection process was conducted in double-blind by two reviewers (SS and BP), who screened all titles, abstracts and full texts independently. Studies were considered if published in English and referred to an adult population (≥18 years old). Studies were included provided that they measured HRQoL or healthcare resources use (or both). Case reports, letters, comments, editorials and non-systematic review were excluded. The inclusion and exclusion criteria are presented in Table 1. Agreement on eligibility was resolved by consensus. Inter-assessor reliability was assessed using a kappa statistic (considered slight for values from 0 to <0.2, fair from 0.2 to 0.4, moderate from 0.4 to <0.6, substantial from 0.6 to <0.8 and almost perfect from 0.8 to 1). Data were extracted using a customized template based on the PICOS statement by one reviewer and verified by a second reviewer.

2.3. Quality assessment

The methodological quality of studies included was assessed using the Cochrane recommendations and the criteria suggested by the Centre for Reviews and Dissemination (CRD) guidance for conducting systematic reviews in healthcare (Higgins and Green, 2011; CRD, 2009). These criteria were modified in order to reflect the needs of this review; data were extracted by one reviewer and checked by a second reviewer. In addition, the Drummond 35 items check-list was used to assess the quality of economic studies (Drummond and Jefferson, 1996).

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