Critical Reviews in Oncology/Hematology 112 (2017) 113–125

Contents lists available at ScienceDirect

Critical Reviews in Oncology/Hematology

journal homepage: www.elsevier.com/locate/critrevonc

Efficacy and safety of olanzapine for the prevention of chemotherapy-induced nausea and vomiting: A systematic review and meta-analysis

Jukapun Yoodee, Unchalee Permsuwan, Mantiwee Nimworapan *

Faculty of Pharmacy, Chiang Mai University,Suthep Road, Muang District, Chiang Mai, 50200, Thailand

Contents

ARTICLE INFO

Article history:
Received 1 November 2016
Received in revised form 8 February 2017
Accepted 14 February 2017

Keywords:
Olanzapine
Chemotherapy-induced nausea and vomiting
Antiemetic
Meta-analysis
Systemic review

ABSTRACT

Background: Olanzapine is an anti-psychotic drug that has been used for preventing and treating Chemotherapy-Induced Nausea and Vomiting (CINV). This study aimed to systematically review and meta-analyze the efficacy and safety of olanzapine for prophylaxis and treatment of CINV.
Methods: We conducted a systematic literature search of MEDLINE, EMBASE, SCOPUS, and the Cochrane Central Register of Controlled Trials—CENTRAL up to July 15, 2016. All observational and intervention studies were included, but only the intervention studies were pooled for meta-analysis. The efficacy outcome was the proportion of patients achieving complete response (CR) – no emesis and no rescue therapy, in the acute, delayed, and overall phases. The safety outcomes were the adverse events associated with olanzapine according to Common Terminology Criteria for Adverse Events (CTCAE).
Results: Sixteen studies were eligible: 15 clinical trials and 1 observational study. Nine of the interventional studies were pooled for meta-analysis. The CR of olanzapine was superior to other anti-emetic regimens, in both the delayed and overall phases (RR = 1.27, 95% CI 1.07–1.49, RR = 1.32, 95% CI 1.08–1.62, respectively). However, olanzapine was not better than standard CINV prophylaxis of the nausea and emesis outcome in the acute phase. Drowsiness and constipation were the most reported adverse events. No grade 3 or 4 adverse events were reported.
Conclusion: Olanzapine is effective and safe at reducing during the delayed and overall phase of the CINV prevention. Other regimens might be added, in cases of CINV during the acute phase of CINV.

* Corresponding author at: Department of Pharmaceutical Care, Faculty of Pharmacy, Chiang Mai University, Chiang Mai, 50200, Thailand.
E-mail address: mantiwee@gmail.com (M. Nimworapan).

http://dx.doi.org/10.1016/j.critrevonc.2017.02.017
1040-8428/

1. Introduction

Chemotherapy-induced nausea and vomiting (CINV) is a major adverse event of cancer chemotherapy (Laszlo and Lucas, 1981; Teunissen et al., 2007; Osoba et al., 1997; Bloechl-Daum et al., 2006; Sommariva et al., 2016; Tageja and Groninger, 2016). CINV can significantly deteriorate a patient's quality of life, lead to poor adherence to cancer treatment, and result in severe clinical conditions, such as dehydration, electrolyte imbalance, and malnutrition (Osoba et al., 1997; Tageja and Groninger, 2016; Morrow et al., 1991). In addition, the uncontrolled CINV can cause treatment failure or poor treatment response in cancer patients (Laszlo and Lucas, 1981; Tageja and Groninger, 2016; Rao and Faso, 2012; Bayo et al., 2012; Grunberg, 2012).

The development of CINV varies among individuals, depending on several factors (Tageja and Groninger, 2016; NCCN, 2015; Hesketh et al., 2016). One of the most important factors is the emetogenicity of the chemotherapy (Bayo et al., 2012; NCCN, 2015). Cancer patients receiving highly emetogenic chemotherapy (HEC) are expected to have CINV in more than 90% of chemotherapy sessions, if prophylactic antiemetics is not administered. Moderate emetogenic chemotherapy (MEC), without prophylaxis, induces CINV to a lesser extent (Bayo et al., 2012; NCCN, 2015; Hesketh et al., 2016).

The National Comprehensive Cancer Network (NCCN) currently recommends four categories of emetogenic potential for parenteral chemotherapeutics: high emetic risk (90% of patients experience acute emesis), moderate emetic risk (30–90%), low emetic risk (10–30%), and very low emetic risk (<10%) (Roila et al., 2010). The NCCN guidelines suggest preventing CINV in cancer patients with HEC and/or MEC with a combination of neurokinin (NK1), serotonin (5-HT3) receptor antagonist, and dexamethasone (Tageja and Groninger, 2016; NCCN, 2015; Hesketh et al., 2016). Breakthrough CINV, which occurs despite adequate antiemetic prophylaxis, however, remains a significant problem (Grunberg et al., 2004; Hickok et al., 2003). The NCCN guidelines recommend treating breakthrough CINV with a different agent used in the prophylactic regimen, and continuing the breakthrough medication, if this controls nausea and vomiting (Teunissen et al., 2007; Grunberg, 2012; NCCN, 2015).

Olanzapine is an atypical antipsychotic agent of the thienobenzodiazepine class. It blocks multiple neurotransmitter receptors, including the D2 and 5-HT_3 receptors, which appear to be involved in nausea and emesis. Therefore, it may have significant antiemetic properties (Navari, 2009; Brafford and Olanzapine, 2014). The use of olanzapine in combination with other 5-HT_3 receptor antagonists and dexamethasone in adult cancer patients has recently shown promising results in preventing CINV and/or breakthrough emesis (DeRemer et al., 2016; Chiu et al., 2016; Chow et al., 2016). It also has been shown in meta-analysis studies by Wang et al. (Wang et al., 2014) and Chiu et al. (Chiu et al., 2016) that olanzapine is more efficacious than other standard antiemetics for the rescue of CINV. However, these two studies did not include the most recent clinical trials that were published in 2016 (Babu et al., 2016; Navari et al., 2016). Hence, we aimed to conduct a systematic review and to compare the efficacy and safety of olanzapine and other standard antiemetics for prophylaxis and treatment of CINV.

2. Methods

2.1. Search strategy

We searched for both intervention and observational studies that evaluated the efficacy and safety of olanzapine, either as monotherapy or add-on therapy, in treating and preventing CINV. We performed an electronic database search of MEDLINE, EMBASE, SCOPUS, and the Cochrane Central Register of Controlled Trials—CENTRAL from their inception to July 15, 2016.

We used a wide search strategy, with the following keyword combinations: "olanzapine"; OR "thiobenzodiazepine"; OR "Zyprexa"; AND "chemotherapy-induced nausea and vomiting"; AND "CINV"; OR "nausea in cancer patients"; OR "vomiting in cancer patients." Furthermore; we also considered the reference lists of all searched studies.

2.2. Selection criteria and data extraction

Two reviewers independently screened titles and abstracts, which were identified from the search strategy, to select studies based on the inclusion criteria. Those criteria included study population, intervention, and outcome. The studies of interest were those that reported either olanzapine as add-on treatment (dexamethasone plus 5-HT3 antagonist, with or without NK1 antagonist) or olanzapine monotherapy compared to standard treatment. We excluded non-English-language studies and duplicate articles found in each database.

We extracted data regarding general information (such as author affiliation and funding source) and study characteristics (such as study design, study population, treatment, and duration of treatment); and outcomes. Extracted data were grouped such that information for different treatment strategies could be easily identified. Any disagreement between reviewers was discussed until a consensus was reached.

2.3. Outcomes of interest

The primary outcomes in this study were complete response (CR), no emesis and no rescue therapy. A CR was defined as the absence of vomiting and the absence of the need for rescue antiemetic drugs. If no emesis or no rescue therapy was not reported in the study, the events of no emesis were assumed similar to complete response. The duration of primary outcome occurrence was also considered, and classified as either acute phase (0–24 h after chemotherapy), delay phase (24–120 h after chemotherapy), or overall phase (0–120 h after chemotherapy). If overall response was not reported, we assumed it to be the lowest percentage of either the acute or delayed responses.

The secondary outcome was the reported adverse events associated with olanzapine treatment according to the Common Terminology Criteria for Adverse Events (CTCAE). Outcome measurement was also described.

2.4. Statistical analysis

STATA® data analysis and Statistical software version 14 (Serial number: 301406219300) were used to analyze the data. For the primary endpoints, studies were stratified based on setting prophylaxis or treatment. The Mantel-Haenszel random-effects method was used to generate risk ratios (RR) and the corresponding 95% confidence intervals (CIs). The statistical heterogeneity of trial results was assessed by the χ^2 test and expressed as I^2 plus the corresponding P value. Heterogeneity was considered if the I^2 and P values were more than 50% and 0.05, respectively. The publication bias was estimated by the "Trim and Fill" method; the result was displayed as a funnel plot.

3. Results

3.1. Characteristics of included studies

Based on our literature search of the four databases mentioned above, 573 studies were identified; we excluded 371 duplicates.