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Control nausea and vomiting during chemotherapy in pregnant women with non-small cell lung cancer

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SUMMARY

AUTHORS' CONTRIBUTION: (A) Study Design · **(B)** Data Collection . **(C)** Statistical Analysis · **(D)** Data Interpretation · **(E)** Manuscript Preparation · **(F)** Literature Search · **(G)** No Fund Collection

Background: Chemotherapy-Induced Nausea and Vomiting (CINV) seriously affect cancer patients both physically and emotionally, therefore compromising their quality of life and maybe discouraging more treatment. The several kinds of CINV need for varied treatment schedules, usually involving corticosteroids, 5-HT3 receptor antagonist, and NK1 receptor antagonist.

Methods: 150 pregnant women with non-small cell Lung Cancer were divided into Five groups: 1st group administer Ondansetron (OND); 2nd group administered Dexamethasone (Dex); 3rd group administered Metoclopramide (Met); 4th group on combination OND plus Dex and 5th group on Aprepitant plus Dexamethasone (Apr+Dex). the main objective was to assess the percentage of patients experiencing total CINV within each group.

Results: Of the 150 women, 71 (44%) received MEC and 90 (56%) received HEC. The 4th group showed 60% Complete Control, 13% Complete Protection, and 27% Complete Response which consider better results and remarkable degree of protection as compared with other groups. 1st and 2nd groups showed non-significant difference (p>0.05).

Conclusion: The results of the study led to guidelines for the use of serotonin and corticosteroids to prevent CINV in patients with NSCLC undergoing chemotherapy.

Keywords: Chemotherapy; Pregnant women; Lung cancer

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INTRODUCTION

The medulla oblongata's Vomiting Center (VC) is responsible for coordinating the vomiting reaction. This is achieved by the VC combining a spectrum of peripheral and central impulses, which are known as the peripheral and central pathways, respectively [1]. *Via* the peripheral pathway, abdominal vagal afferents transmit stimuli including pharyngeal stimulation and stomach/ duodenal distension [2]. Abdominal vagal afferent fibers express many receptors including 5-HT3, Neurokinin (NK) 1, and cholecystokinin-1, which can induce the emetic reaction. The main arbiter of this reaction is 5-HT3 [3]. The symptoms of Chemotherapy-Induced Nausea and Vomiting (CINV) may manifest at various stages of the treatment regimen. Immediate CINV, which is characterized by vomiting within 24 hours of the initial administration of chemotherapy, is primarily mediated by 5-HT3 receptors [4] Delayed Chemotherapy-Induced Nausea and Vomiting (CINV) occurs between 24 and 5 hours following chemotherapy and is largely mediated by substance P binding to NK1 receptors in the central nervous system [5].

AIM

The purpose of the study is to examine the reliability and effectiveness of antiemetic medicines in the treatment of NSCLC during pregnancy.

METHOD

The prospective study enrolling 150 pregnant women with NSCLC stage 2 from different government hospitals. The women were divided into five groups depend on type of antiemetic medication; 1st group administration ONS 8 mg IV for acute and 8 mg for orally for delay phase; 2nd group administration Dex 8 mg IV and 0.5 mg orally; 3rd group Met 10mg IV and 10 mg orally; 4th group administration combination ONS plus Dex 8mg plus 8 mg for IV and 8 mg plus 0.5mg for oral; and 5th group administration aprepitant plus Dex130 mg IV plus 0.5 mg and 125 mg orally plus 0.5 mg.

Exclusion criteria was history of alcohol consumption, their history of motion sickness or pregnancy-related vomiting

Acute NV was defined by a Likert score of at least 1 for nausea or vomiting on day 1 (chemotherapy) and delayed NV by any day between days 1 and 7 after chemotherapy. Investigators used the National Cancer Institute Common Terminology Criteria for Adverse Events (version 3) to evaluate vomiting events [6].

Statistical analysis

This study used descriptive analysis. The sample's demographics, clinical features, incidence and severity of delayed emesis, number of emetic episodes, and time till emesis were summarized using descriptive statistics. The chi-squared test was used to compare delayed nausea and vomiting in men and women. Multivariate logistic regression was also performed to examine how additional clinical and demographic factors affect delayed emesis rates.

RESULTS

Patients' demographics properties

This study enrolled 150 people between October 2023 and January 2024. Included in the study were 100 patients (66.67%) who received HEC and 50 (33.33%) who received MEC (**Tab. 1.**).

Antiemetic regimens

The rate of MEC induced acute emesis on day 1 as reported by the patients on their diary card can be seen in **Tab. 2.** and **Fig. 1.** Ondansetron plus corticosteroid combination was administered to 95.5% of patients during acute emesis, indicating a high level of protection against this phase. This rate is similar to that of patients treated with Aprepitant plus corticosteroid combination (87.2%). When it came to controlling acute emesis, there was no significant difference (p>0.05) between the combinations of aprepitant with corticosteroid, dexamethasone alone (83.7%), and ondansetron alone (83.4%). Nonetheless, there was insignificant difference (p>0.05) between the acute and delay phases in the management of acute emesis.

The endpoints of the all-patient groups, complete response, complete protection, and complete control were examined. The findings showed that, for delayed (days 2-7) antiemetic medication, patients that took single medication as Dexamethasone our results showed that there is insignificantly difference (p>0.05) between it and Ondansetron while we found higher proportion of both medications when compared with Metoclopramide to achieve delayed complete control (40% and 37% *vs.* 20%, P=0.003). prior to adjusting for measured confounders statistically, patients taking Ondansetron or Dexamethasone alone were approximately 1.3-1.8 times more likely to exhibit delayed complete control than patients taking Metoclopramide (unadjusted odds ratio [OR]=1.25, 1.83 respectively. 95% confidence interval [CI]=-31.61 to 31.61).

On another hand, we noticed that the combination of Ondansetron with Dexamethasone exhibits higher percent

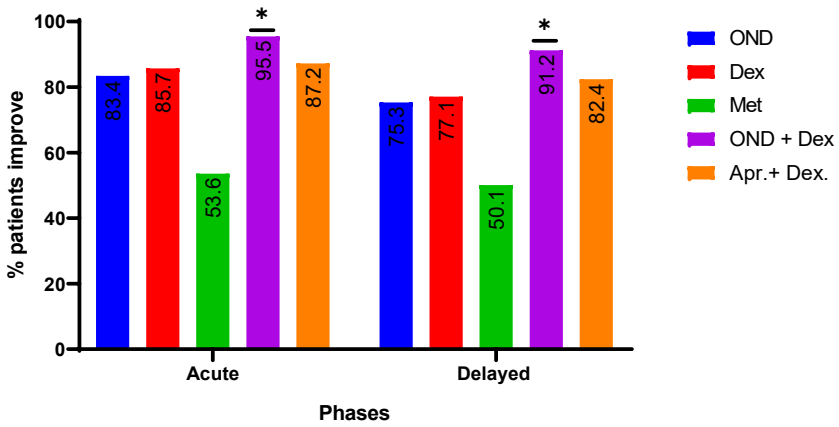
Tab. 1. Demographic specifications of the patients undergoing CT (n=150).

Characteristics	% (n)	*P* Value
Age (years)		
20 to 40 years	28 (42)	0.033
41 to 60 years	72 (108)	
Marital status		
Single	20 (30)	0.022
Married	80 (120)	
Pearson chi-square and Fisher's exact tests were used for variables measured on a nominal scale; chi-square linear-by-linear association tests were used for variables measured on an ordinal scale.		

Tab. 2. Percentage of acute and delayed emesis by chemotherapeutic agents.

Category	OND *n*=41	Dex. *n*=30	Met. *n*=30	OND + Dex *n*=30	Apr.+ Dex. *n*=30	P value
Acute (<24 hr) (day 1)	83.4	85.7	53.6	95.5*	87.2	0.002
Delayed (>24 hr) (days 2–7)	75.3	77.1	50.1	91.2*	82.4	0.005

Fig. 1. Comprise between acute and delayed phases and efficacy of anti-emetic drugs.

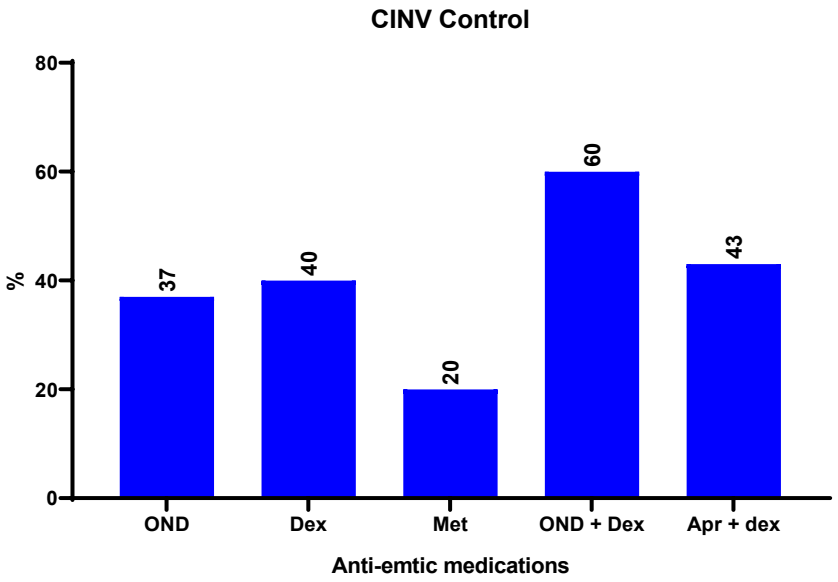


Tab. 3. CINV control.

Protocol	Administration	Complete Control	Complete Protection	Complete Response
Ondansetron (A)	MEC *n*=41	15 (37%)	9 (22%)	17 (41%)
Dexamethasone (B)	MEC *n*=30	12 (40%)	7 (23%)	11 (37%)
Metoclopramide (C)	MEC *n*=30	6 (20%)	11 (37%)	13 (43%)
Ondansetron + Dexamethasone (D)	MEC *n*=30	18 (60%)	4 (13%)	8 (27%)
Aprepitant + dexamethasone (E)	MEC *n*=30	13 (43%)	8 (27%)	9 (30%)

The degree of control of CINV was defined in 3 categories that were not mutually exclusive: (a) complete response= no emetic episodes and no rescue therapy; (b) complete protection= no emetic episodes, no rescue therapy, and no significant nausea (Likert score 2 or less); and (c) complete control= no emetic episodes, no rescue therapy, and no nausea.

Fig. 2. Compare the efficacy of complete control between anti-emetic medication.



of complete control when compared with Aprepitant plus dexamethasone combination (60% *vs*. 43%) (Unadjusted odds ratio [OR]=1.4. 95% confidence interval [CI]=-11.21 to 21.23) (**Tab. 3.** and **Fig. 2.**).

DISCUSSION

Since CINV is a serious adverse reaction to chemotherapy, accurately estimating the likelihood of its occurrence is crucial. Our research consistently showed that accurately predicting whether a patient will experience CINV after receiving HEC or MEC is challenging. As a result, we recommend following current guidelines and not reducing antiemetics. However, despite confirming previously reported risk factors for CINV, our study did not identify sufficient predictors. We consistently found that younger age was a risk factor for acute nausea, acute vomiting, and delayed nausea, aligning with findings from previous research.

The study's findings indicate that in the acute phase, approximately half of the patients who received HEC reported CINV, whereas in the delayed phase, more than half of them experienced nausea. According to the Likert scale for the severity of CINV, we observed that the score was high on the first day and gradually declined until the seventh day, while the score was zero during the delay phase and gradually increased until the seventh day, when the maximum score was recorded.

There is still a need for effective treatment of nausea during both the immediate and prolonged periods in patients who receive High Emetogenic Chemotherapy (HEC) and Moderately Emetogenic Chemotherapy (MEC) [7]. Even though use the single drug such as NK-1 receptor antagonist alone or a 5-HT 3 receptor antagonist or combination, dexamethasone has demonstrated advantages in patients undergoing high emetogenic chemotherapy with cisplatin or cyclophosphamide-doxorubicin [8,9].

We found that combination of serotonin receptor antagonists in combination with DEX had highly efficacy in reduce CINV as compared with other anti-emetics while other studies investigated controversial, Herrington, et al. conducted a comparison trial with aprepitant, palonosetron, and DEX alone, There were found that no significant differences in emesis or nausea which aligns with our study findings [10]. Kang, et al. found that oral aprepitant, combined with ondansetron, with or without DEX, effectively prevents chemotherapy-induced nausea and vomiting in patients undergoing chemotherapy, compared to controls or those treated only with ondansetron, with or without DEX [11].

CONCLUSION

The combination of Ondansetron with corticosteroids is considered a standard treatment regimen for preventing CINV in patients with NSCLC undergoing chemotherapy.

RECOMMENDATION

We recommended that healthcare providers should using Ondansetron with corticosteroids as part of their treatment guideline for chemotherapy induces CINV to minimize the risk.

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