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USEFULNESS OF APREPITANT OVER CONVENTIONAL ANTIEMETIC IN CISPLATIN INDUCED VOMITING –RETROSPECTIVE SINGLE INSTITUTION EXPERIENCE IN TERTIARY CARE CANCER CENTRE

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ABSTRACT

Introduction Chemotherapy induced nausea and vomiting (CIN) one of the troublesome adverse event following chemotherapy especially in cisplatin based. CIN usually managed with ondansetron and corticosteroids which are effective in controlling acute phase but ineffective in delayed vomiting associated with cisplatin. Aprepitant, a drug that antagonizes the effect of substance P on neurokinin type 1 receptor showed promising results in controlling both phases of CINV **Aim of the study** 1. To compare aprepitant with conventional anti emetics which effectively reducing cisplatin based chemotherapy induced vomiting especially delayed phase of vomiting. **Materials and methods** All patients treated with cisplatin in cancer institute, Adyar, chennai from 2013 january to june included in this study. Aprepitant in one arm and using conventional antiemetics in another arm were taken into this study. Those who defaulted are excluded from the study. Another arm ondansetron and corticosteroids were given without aprepitant. All patients weight, electrolytes and cumulative dose were recorded and analysed using standard statistical methods. **Results** Total no of patients included in this study were 190. Among 190 Carcinoma cervix patients were 92 and 98 patients were oral cavity cancers. In this 76 patients were given aprepitant and 114 patients without aprepitant. Nausea experienced by the patients were similar between 2 arms and insignificant (18.4% vs 21.9 %- with and without aprepitant respectively). But significant reduction in CIN grade II & III were noted in aprepitant arm. In the study we recorded that aprepitant effective in preventing severe and delayed CIN than early and acute phase of CIN The loss of weight more than 2 kgs were recorded and found that 18.4 (n=14)% & 64.9 (n=74) respectively in aprepitant and conventional arm(p=0.0001). All patients were monitored for electrolyte imbalance and records showed that significant difference noted between groups(0% Vs 7.8% in aprepitant and conventional arm respectively , p=0.012). **Conclusion** Aprepitant is one of the potent drug reducing CIN and vomiting related complications such as electrolyte imbalance and weight loss. In our study we proved that aprepitant extremely significant in reducing cisplatin based chemotherapy induced vomiting.

KEYWORDS : Aprepitant, CIN, cisplatin induced voming

INTRODUCTION

Chemotherapy induced nausea and vomiting (CIN) one of the troublesome adverse event following chemotherapy especially in cisplatin based. CIN usually managed with ondansetron and corticosteroids which are effective in controlling acute phase but ineffective in delayed vomiting associated with cisplatin. Aprepitant, a drug that antagonizes the effect of substance P on neurokinin type 1 receptor showed promising results in controlling both phases of CINV.

Aim of the study

1. To ensure the apripitant was effective in reducing cisplatin based chemotherapy induced vomiting especially delayed phase of vomiting.

Materials and methods

All patients treated with cisplatin in cancer institute, Adyar, chennai from 2013 january to june included in this study. Aprepitant in one arm and using conventional antiemetics in another arm were taken into this study. Those who defaulted are excluded from the study. Aprepitant was given 120 mgs tablets per orally 30 minutes prior to chemotherapy and 80 was given on day 2 &3 in addition to ondansetron and corticosteroids. Another arm ondansetron and corticosteroids were given without aprepitant. All patients weight, electrolytes and cumulative dose were recorded and analysed using standard statistical methods.

Results

Total no of patients included in this study were 190. Among 190 Carcinoma cervix patients were 92 and 98 patients were oral cavity cancers. In this 76 patients were given aprepitant and 114 patients without aprepitant.

CIN

Nausea experienced by the patients were similar between 2 arms and insignificant (18.4% vs 21.9 %- with and without aprepitant respectively). But significant reduction in CIN grade II & III were noted in aprepitant arm. In the study we recorded that aprepitant effective in preventing severe and delayed CIN than early and acute phase of CIN.

Table-1

		Aprepitant arm	Conventional arm	P value
1	Nausea	14 (18.4%)	25(21.9)	0.58
2	Grade II emesis	17 (22.3%)	55 (48.2%)	0.0004
3	Grade III emesis	1 (1.3%)	40 (35.8%)	0.0001

Weight loss

Weight loss at the end of chemotherapy were recorded and it found to significant reduction in weight loss in aprepitant arm. The loss of weight more than 2 kgs were recorded and found that 18.4 (n=14)% & 64.9 (n=74) respectively in aprepitant and conventional arm(p=0.0001).

Electrolyte imbalance

All patients were monitored for electrolyte imbalance and records showed that significant difference noted between groups(0% Vs 7.8% in aprepitant and conventional arm respectively , p=0.012).

DISCUSSION

Pathophysiology of vomiting

The emetic response is primarily a protective reflex that occurs after the ingestion of toxic substances, after certain surgical procedures and as a consequence of a wide variety of diseases. Vomiting is a complex reflex mechanism which involves afferent and efferent pathways and a vomiting center (VC). VC is considered to be situated with in the medulla

oblongata of the brain stem.[6] VC has mainly three components, area postrema (AP), nucleus tractus solitarius (NTS) and dorsal motor vagal nucleus (DMVN), which integrates the emetic responses.[6]

Anticancer drugs can cause release of serotonin and substance P from the enterochromaffin cells of gastric mucosa, which sends impulses to the VC through the vagal afferent nerve fibers that innervate the gastrointestinal tract (GIT). Disturbances in the vestibular apparatus will also stimulate VC to produce an emetic reflex.[7] Followed by the stimulation of VC, vomiting is then mediated by various efferent pathways including the vagus and phrenic nerves.[6]

Role of neurotransmitters

Emesis is primarily mediated through neurotransmitters in the central nervous system and the GIT. Among them serotonin, dopamine, substance P, acetylcholine and histamine are well known in this regard.[8] Therefore, in the treatment of CINV, the antagonists of these neurotransmitter receptors are well-explored and serotonin receptor antagonists remain as the mainstay of treatment with or with out corticosteroids.

The early clinical trials with aprepitant showed promising results in preventing CINV, notably in delayed emesis than acute emesis compared with $5HT_3$ antagonists in patients receiving cisplatin.[1-3]. Thus it also reduces the complication related to CIN like electrolyte imbalance, weight loss.

In our study also found that aprepitant effectively suppressing delayed emesis than acute or early phase of vomiting.

A randomized, double blind, placebo controlled trial conducted in Latin America evaluated the efficacy and tolerability of aprepitant plus standard therapy in 569 cancer patients scheduled to receive treatment with high dose cisplatin. The complete response rate was significantly high in aprepitant group at day 1 (82.8 Vs 68.4%, $P<0.001$) and days 2-5 (67.7 Vs 48.6%, $P<0.001$) with similar adverse events in both groups (72.8 vs. 72.6%).[4]

Herrstedt et al in preventing CINV by moderately, emetogenic chemotherapy (cyclophosphamide alone or with dexamethasone or epirubicin) over multiple cycles.[5]

CONCLUSION

Aprepitant is one of the potent drug reducing CIN and vomiting related complications such as electrolyte imbalance and weight loss. In our study we proved that aprepitant extremely significant in reducing cisplatin based chemotherapy induced vomiting.

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