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EFFECT OF ORAL GRANISETRON IN IMPROVING QUALITY OF LIFE AS COMPARED TO OTHER 5HT-3 ANTAGONISTS IN DELAYED CINV IN PATIENTS OF BREAST CANCER

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ABSTRACT

Introduction: The primary objective was to prevent delayed chemo induced nausea and vomiting (CINV). The primary efficacy end point was complete response (CR) and improving quality of life (QOL).

Material and Method: This is a prospective, observational study conducted on 120 previously untreated histopathologically-proven patients of ductal carcinoma of Breast from July 2015 to March 2016. In this study the patients were selected based on our inclusion criteria and each cohort was composed of 40 breast carcinoma diagnosed patients, each cohort receiving Oral Ondansetron 4 mg TDS was given in cohort 1; Oral Granisetron 1 mg BD given to cohort 2 patients; and Oral Palonosetron 0.5 mg OD given to the cohort 3 from day 3 to day 7 post chemotherapy for prevention of delayed CINV, and were asked to keep a vomiting diary , interviewed on telephone and on next follow up visit and then result were graded according to the response obtained by each individual. Patients with history of allergy to 5HT-3 antagonists, any associated medical condition causing nausea/vomiting were excluded.

Results: A total 120 patients were included in the study. In these study 57% patients in Ondanseteron cohort had complete Response, 84% patients in Graniseteron cohort had complete Response and 64% patients in palonosetron cohort had complete response.

Conclusion: As compared to other 5HT3 receptor antagonists, Granisetron has better response in prevention of chemotherapy induced nausea and vomiting in patients of ductal carcinoma breast receiving Anthracyclines based chemotherapy.

KEYWORDS : breast carcinoma, delayed CINV,oral antiemetic,quality of life

INTRODUCTION

Nausea and vomiting result in metabolic imbalances, degeneration of self-care and functional ability, nutrient depletion, anorexia, decline of performance and mental status, wound dehiscence, oesophageal tears, and withdrawal from potentially useful or curative anticancer treatment [1]. Thus chemotherapy induced nausea and vomiting (CINV) compromises the quality of life (QOL) of the patients and reduces treatment compliance [2].

Multi agent regimens are considered standard practice over single agent regimens, and the Early Breast Cancer Trialist Collaborative Group overview has confirmed the improved recurrence and survival outcome observed with Anthracyclines based regimens for management of breast carcinoma [3] which is moderately emetogenic. Since their introduction into routine clinical practice, 5-HT3 receptor antagonists (RAs) have become the cornerstone of current antiemetic prophylaxis and are an integral part of preventive strategies for CINV[4,5].

This study was undertaken with the primary objective of preventing delayed CINV with the aim of achieving complete Response (CR) and improving QOL.

MATERIAL AND METHODS

The study design was that of prospective, observational study conducted on previously untreated 120 patients of histopathologically proven ductal carcinoma of Breast, who had attended Department of Radiotherapy, Gandhi Medical College and Hamidiya Hospital, Bhopal from July 2015 to March 2016. Inclusion criteria for the study:

1) Patients with age less than 70 years, both sexes
2) Histologically proven cases of ductal carcinoma
3) Karnofsky performance score/scale less than or equal to 70
4) Normal haematological, renal, liver function tests and normal chest X ray.

Exclusion criteria for the study was:

1) Age more than 70yrs
2) Prior irradiation or surgery
3) Histology other than ductal carcinoma

Anthracyclines based chemotherapy for breast cancer which is moderately emetogenic was administered to all of the patients. Cyclophosphamide, Adriamycin and 5Fluorouracil were one of the multi-agent regimens used. These patients were divided into three cohorts and each cohort was composed of 40 diagnosed cases of ductal carcinoma breast. All patients were prescribed oral 5HT3 antagonists, Oral Ondansetron 4 mg TDS was given in cohort 1; Oral Granisetron 1 mg BD given to cohort 2 patients; and Oral Palonosetron 0.5 mg OD given to the cohort 3 from day 3 to day 7 post chemotherapy for prevention of delayed CINV. For evaluation patients were asked to keep a vomiting diary, interviewed on telephone and on next follow up visit for episodes of vomiting and how did it affect their daily routine work. Then results were spread on MS EXCEL SHEET and were graded according to the response obtained by each individual. Patients with history of allergy to 5HT-3antagonists, any associated medical condition causing nausea/vomiting was excluded.

Statistical analysis: Data was spread in Microsoft Excel 2010 and analysis was done. Descriptive statistics were performed to determine the mean and standard deviation for demographic data. The level of statistical significance was set at a p-value of 0.05. Group means were compared by independent t-tests and the Chi-squared test of association.

RESULTS

A total of 120 patients of ductal carcinoma breast, receiving chemotherapy were enrolled. Of these, 40 patients received oral Ondansetron 4mg TDS (cohort-1). 40 patients received oral Granisetron 1mg BD (cohort-2) and 40 patients received oral Palonosetron 0.5mg OD (cohort-3) from day 3 to day 7 For Prevention Of Delayed CINV.

The results were analysed on the basis of response obtained from the study subjects. They were graded as complete response when they did not have complaint of nausea and vomiting. Complete response rate was 84% among the patients who received Granisetron ie. Cohort 2, 64% complete response rate among the patients who received Palonosetron ie. Cohort 3, as compared to complete response rate was

57% among the patients who received Ondansetron that is Cohort 1. Thus, as compared to other 5HT3 receptor antagonists, Granisetron has better response in prevention of chemotherapy induced nausea and vomiting in patients of ductal carcinoma breast receiving Anthracyclines based chemotherapy.

- 57% patients in Ondanseteron cohort had complete
- response.
- 84% patients in Graniseteron cohort had complete
- response.
- 64% patients in palonosetron cohort had complete
- response.

DISCUSSION

Poor control of acute CINV is an established predictor for delayed CINV that typically peaks in severity between day 2 and day 4, post chemotherapy, depending on the emetogenic profile of the agents used [6]. Although the severity is decreased in delayed CINV in comparison with acute nausea and vomiting, the course can be more protracted, resulting in significant difficulties with hydration, nutrition, and performance status thus impairing QOL [3].

Vomiting results from stimulation of a multistep reflex pathway controlled by the brain, and is triggered by afferent impulses to the vomiting centre (located in the medulla) from the chemoreceptor trigger zone; pharynx and gastrointestinal tract (by way of vagal afferent fibres); and cerebral cortex. The chemoreceptor trigger zone, vomiting centre, and gastrointestinal tract have many neurotransmitter receptors. Activation of these receptors by chemotherapeutic agents or their metabolites may be responsible for chemotherapy induced emesis. Principal neuroreceptors involved in the emetic response are serotonin 5-hydroxytryptamine (5-HT3) and dopamine receptors other neuroreceptors include acetylcholine, corticosteroid, histamine, cannabinoid, opiate, and neurokinin-1 (NK-1) receptors, which are located in the vomiting and vestibular centres of the brain[1]. Nausea and/or vomiting induced by chemotherapy is commonly classified as acute, delayed, anticipatory, breakthrough, or refractory. Delayed-onset nausea and/or vomiting develop in patients more than 24 hours after chemotherapy is administered and commonly occurs when Cisplatin, Carboplatin, Cyclophosphamide, and/or Doxorubicin are used. In general, to provide maximal protection against chemotherapy-induced emesis, antiemetic therapy should be initiated before chemotherapy and continued for the duration of the emetic activity according to the chemotherapeutic agent being used [1].

To date, Aprepitant and Palonosetron have been reported to exhibit effective delayed antiemetic effects. However, the efficacy of these agents in combination has not been investigated. For acute-phase emesis, the two receptors are associated with vomiting. However, in the case of delayed Emesis, the impact of substance P is considered to become dominant, which is regarded to be a cause for limited antiemetic action of 5-HT3 receptor antagonists for delayed vomiting. Palonosetron and Granisetron are 5-HT3 receptor antagonist antiemetic agents. Palonosetron differs from conventional drug as it has an extremely long half-life in the blood (~40 h), as well as high affinity and selectivity for 5-HT3 receptors. Thus, it has been identified to be efficacious for the treatment of delayed nausea and vomiting, which occur ≥24 h following chemotherapy [7].

The current study provides evidence that Palonosetron given to patients receiving highly emetogenic chemotherapy has clinical and statistical superiority in preventing chemotherapy induced nausea and vomiting as compared to Ondansetron but less effective as Granisetron. In the study, Palonosetron was given in a dose of 0.5mg single dose which was found to be more affective as compared to Ondansetron 4mg thrice a day,64% patients in Palonosetron cohort had complete response as compared to 84% patients in Granisetron (1mg twice a day) cohort who had complete response [6]. Ohzawa et al. also reported that there were no significant differences in the incidence of CINV in breast cancer patients who received Palonosetron and Granisetron [7].

This was against the study done by Chan et al. and Saito et al. where they proved Palonosetron to be superior than Granisetron in preventing CINV[9,10].

Conclusion

Breast cancer constitutes a significant proportion of the patient population in which chemotherapy is commonly indicated. The adjuvant chemotherapies for breast cancer usually involve moderately to highly emetogenic agents and regimens. Since most of the chemotherapy regimens for breast cancer are of moderate emetogenic potential, optimization of an antiemetic regimen would significantly improve QOL and potentially increase patients acceptability and tolerability of chemotherapy, thereby allowing an increase in the completion rate of planned treatment which has been shown to improve survival. In this study, oral Granisetron at a dose of 1mg BD was found to have better response as compared to other 5 HT-3 receptor antagonists. The evaluation of vomiting and nausea is difficult; however, the evaluation of complete response was possible via the use of patient logs and survey.

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