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Original Research Article

Practical insight into the current management of chemotherapy induce nausea and vomiting: An indian survey

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ABSTRACT

Background: Nausea and vomiting are two of the most severe and distressing consequences of cytotoxic chemotherapies. The present survey was conducted to highlight current practice pattern, factors that contribute to failure and to determine current challenges and unmet need in the management of chemotherapy Induce Nausea and vomiting (CINV).
Materials and Methods: The present study was a questionnaire based survey conducted among oncologist/ hematologist and consisted of sample of 16 questions.
Results: 328 oncologist were included in the analysis**,** majority (57%) being medical oncologist. CINV leading to dose reduction, delay or discontinuation was seen in 28% of the practioners with more than 10% in their usual practice. Breakthrough nausea and vomiting was the most common type of CINV experienced by patient on chemotherapy. Controlling CINV in delayed phase was the greatest perceived challenge by 62% respondents. In both Highly emetogenic chemotherapy (HEC) and moderately emetogenic chemotherapy (MEC) setting, serotonin receptor antagonists (5HT3 RA) was the most preferred drug in both acute and delayed phase. NCCN was the most preferred guideline in 69% respondents. Ninty for percent of the respondent believed that there is a need for better drug in the management of CINV and the new drug should have superior efficacy, better control of delayed phase and single dose administration before chemotherapy.
Conclusion: Survey highlights the need for better contorl of delayed phase of CINV and the need for drug with better efficacy in delayed phase with single dose administration.
Key message: The survey highlights unmet need and poor control in the management of delayed phase of nausea and vomiting. Also, majority of the oncologist felt the need for a new drug in the management of CINV.

1. Introduction

Nausea-vomiting are two of the most severe and distressing consequences of cytotoxic chemotherapies. With new advent and improvement in the anti-emetic drugs and guidelines there has been improvement in the control of nausea and vomiting but CINV still occurs in approximately 50% of patients receiving cancer chemotherapy.[1] Vomiting is largely well controlled but nausea, both acute and delayed, is still a significant problem in more than half of patients receiving highly or moderately emetogenic chemotherapy.[1] Anticipatory nausea is another big problem. A 2016 study showed that every 1-mm increase in anticipatory nausea on the visual analog scale was significantly associated with a 2% to 13% increase in the likelihood of chemotherapy-induced nausea and vomiting.[2] Thus, CINV is not only distressing to patients, but also lead to complication such as dehydration, electrolyte imbalance, weight loss and malnutrition, which may sometimes result in emergency room visit and will add additional cost.[3–5]

CINV perception also differs significantly between patients and healthcare providers, in a

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qualitative assessment, severe and uncontrolled nausea, vomiting was ranked slashed to death by patients[6] but according to nurses survey conducted, more than 75% of health care physician underestimate the severity and incidence of nausea and vomiting.[7] Previous studies have also shown suboptimal adherence to antiemetic guideline.[1,8–10]

The present survey was to determine the adherence to guidelines, difficulty in application and unmet need for CINV management in India

2. Materials and Methods

The present study was a questionnaire based survey conducted among oncologist/ hematologist, in April –May 2018. The survey consists of 16 questions, which were validated from a senior oncologist before starting the survey and focused mainly on the challenges and unmet need in the management of CINV. The anonymity and confidentiality was maintained. The responses to the question were compiled in Microsoft excel version 2015 and analysed and accordingly results were prepared. Since, no patient data was involved in the study, this methodology does not require ethics committee approval.

3. Results

Among the 350 oncologist, who were approached to participate in the survey, 328 returned the completely filled form and were included in the analysis. Among 328 respondents, 57% were medical oncologist, 20% were radiation oncologist and the remaining 23% were surgical oncologist (13%) and hematologist (10%). Forty nine percent of respondent reported <50% of their patient had CINV optimally controlled (i.e., experienced complete response [no emesis/no rescue]) with current available antiemetics. Twenty eight percent of respondents reported > 10% of their patients had chemotherapy delayed, discontinued, or dose-reduced due to CINV. Sixty five percent respondent reported having patients requiring emergency department visits or hospitalizations due to poorly controlled CINV during the course of treatment. Breakthrough nausea and vomiting was the most common type of CINV experienced by patient on chemotherapy, this was reported by 62% respondents. Controlling CINV in delayed phase was the greatest perceived challenges by 53% respondents, among them controlling delayed nausea was the most difficult phase as compared to vomiting. Cost and patient compliance were the two most important barriers reported by respondents for optimal management of CINV. Intravenous route was the preferred choice by 83% respondents because of convenience to patient and physician. The greatest perceived challenges or unmet needs in preventing and managing CINV within the respondents' practices were reported as controlling CINV in the delayed phase (62%) and the impact of CINV on patients' quality of life (QoL) (54%). The least significant challenge was institutional policies (5%).

In both HEC and MEC setting, 5HT3 RA was the most preferred drug in both acute and delayed phase. In HEC setting, Neurokinin 1 receptor antagonist (NK1RA) was preferred by 42% on day 1 and by 37% in day 2 and beyond, whereas in MEC setting 35% respondent preferred it on day 1 and 23% on day 2 and beyond. NK1RA (Aprepitant) was the preferred choice of agent by 56% respondents for managing refractory CINV. 94% respondent follow some guideline in the clinical practice, among them, NCCN was the most preferred in 69% respondent. Physician preference was perceived by respondents (36%) as the predominant barrier interfering with use of guideline-recommended antiemetic prophylaxis. Ninty four percent of the respondent believed that there is a need for better drug in the management of CINV and the new drug should have superior efficacy, better control of delayed phase and single dose administration before chemotherapy.

4. Discussion

This pan- India survey highlighted the current state of practice and challenges in the management of CINV. The current evidence suggests, CINV is still an oncologist nightmare, even after 25 years of active clinical research in anti-emesis.[11] The survey was carried among diverse group of healthcare provider who have experience in practicing chemotherapy. Almost half of the respondents reported >50% of their patient does not attend complete response with the available antiemetic therapies. Report available from previous study[12] highlighted, the importance of recognizing the patient and chemotherapy related risk factors in deciding the final anti emetic regimen. Recent NCCN guideline[13] thus recognised the importance of adding an NK1RA in patients with MEC if additional risk factors like young age, female gender, anxiety and previous history of motion or morning sickness is present. The final choice of antiemetic regimen should be based on the combined emetogenic potential of chemotherapy and patient related factor.

Majority of the respondents (79%) agreed that they came across patients who had chemotherapy stopped or changed or postponed due to uncontrolled CINV, of which, 28% respondents had >10% of such patients, this can be because of the severe distress and disruption of daily living which lead patients to consider about change in chemotherapy. This finding was also highlighted in an internet based survey,[14] conducted among physician and nurses, where 32% of healthcare provider had chemotherapy stopped or delayed due to CINV. Severe distress or weakness may also lead to frequent emergency room visit, this was also reported in our survey, where 65% of respondent agreed that some of their patients had to visit emergency department

because of uncontrolled CINV. Pharmacoeconomic study[15] compared the monthly medical cost of patients with uncontrolled and controlled CINV and reported significant increase ($p<0.0001$) in monthly cost to patients with uncontrolled CINV, mainly because of emergency room visits, need of rescue medication, hydration therapy and some additional supportive care. This resource utilization adds to the cost of the therapy and will also add to the indirect cost to the patient in the form of traveling and daily wage lost.

The importance of controlling nausea and vomiting was highlighted in study conducted by Molassiotis A.et al.[16] where uncontrolled CINV in 1st cycle increase the incidence of nausea – vomiting by almost 6.5 time in cycle 2 and almost 14 times in cycle 3. Thus breakthrough nausea and vomiting in cycle 1 increases the anticipation in next and subsequent cycles. Anticipatory nausea-vomiting hampers the patietns willingness to continues the therapy. Breakthrough nausea and vomiting was reported as the most common type among our study participants followed by anticipatory nausea and vomiting. Among the various reasons highlighted for breakthrough CINV, the most important was underestimeting the emetogenic potential of chemotherapy and using weaker anti-emetic regimen to prevent CINV. It thus highlights the need to effectively categorize chemotherapeutic agents according to the emetogenic portential, as categorised by guideline and accordingly to prophylactically prevent CINV with proper anti emetic regimen with higher potency and efficacy.

Delayed phase of nausea and vomiting was considered as the greatest challenge in the management of CINV by 53% respondents in our survey. Among the two, nausea was reported as difficult to control in both acute and delayed phase,but,more in delayed phase. Not only controlling delayed phase but preventing its impacty on quality of life was perceived as a major challenge or unmet need by 54% respondents in our survey. Similar result was highlighted in survey conducted among oncology nurses[1] where controlling delayed phase and its impact on quality of life was the greatest persued challenge. The major challenge managing the delayed phase, as highlighted by Aapro M et al,[11] was home administration of anti emetics, where approximately one third of patients either missed/delayed the dose or make some administration mistake, this non- adherence was perceived as a major challenge by oncologist. The study also highlighted the potential benefit of silimpying the anti emetic regimen and single oral once on day 1 was considered as the solution to the problem by 69% oncologist in the study.[11] Reducing pill burden by using a fixed dose combination agent can improve patients adherence and this is highlighted in various other disease like diabetes, hypertension and HIV.[17–19]

Considering the management of CINV, majority of the respondents preferred using 5 HT3 RA and NK1 RA in the management of acute and delayed phase of CINV in HEC regimen. But our survey also highlights over utilization of 5 HT3RA in delayed phase and underutilization of NK1 RA on day 1 -5 and dexamethsone in delayed phase of CINV. This was seen as a major discrepancy, as NCCN guideline[13] recommends the use of 5 HT3 on day 1, dexamethasone on day 1-4 and a NK1 RA on day 2-3 if oral aprepitant was used on day 1 in HEC regimen. In MEC setting, 5HT3 RA along with NK1 RA was the preferred choice for acute and delayed phase. For delayed phase overutilization of 5HT3 RA along with underutilization of dexamethasone was seen. The increase use of benzodiazepine (10%) day 2 onwards was also inconsistant with guideline. This inconsistency in the guideline recommendation and practise followed was also highlighted in nurses survey[1] and the major reason highlighted for this discrepancy was physicians preference. The PEER study[1] reported the importance of guideline consistency and outcome in the management of CINV, where, guideline adherence improved the complete response rate significantly ($p=0.008$) in patients who were given treatment according to the guideline.

Even after years of availability and clinical research of molecules in the management of CINV, 94% respondents believed there is still a need of better anti emetic drug than the present available Aprepitant, Fosaprepitant, dexamethasone, palanosetron, ondansetron and granisetron in the mangement of CINV. Among the potential property of molecules needed in future, molecule with superior efficacy, single dose administration and better controlled on delayed phase were the most important requirement highlighted in our survey. Among the available antiemetics in India, varioius regime are used in the mangement of CINV, they all differ in the complexicity depending on the route of administration, number of pills required and multiple days of treatment. Rolapitant and NEPA (fixed dose combination of Netupitant and Palanosetron) have longest half-life among the FDA approved NK1RA. With Rolapitant, administration of 5HT3RA needs to be given as a seperate medication. NEPA is administered as an oral capsule one hour prior to chemotherapy. Being a fixed dose combination of NK1RA and 5HT3RA, it does not require repeated administration of 5HT3RA and because of longer half life of netupitant (t1/2= 96hrs) and palanosetron (t1/2=48hrs) it does not require repeated administration during day 1-5 of chemotherapy, thus avoiding home administartion and improving compliance and adherence to the therapy.[20,21] Also· NEPA require lower number of drugs to be administration from day 1-5 after chemotherapy, thus simplifying the anti emetic regimen.[21]

5. Conclusion

Our survey highlights the need for better control of delayed phase of CINV, adherence to the antiemetic guideline in managing CINV and the need for drug with better efficacy

in delayed phase with single dose administration.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare that there is no conflict of interest.

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