

Assessment of Frequency and Severity of ADRS Related with CHOP Therapy in Lymphoma Treatment

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ABSTRACT

Background: Lymphoma a blood related cancer usually treated by using combination of various chemotherapeutic agents, one of the common treatments is CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone).

Objective: Objective of this study was to identify frequency and severity of ADRs affecting various systems due to CHOP therapy from which patients are suffering, so that proper health strategy can be designed to overcome them.

Methodology: study conducted was a prospective, observational enrolled 100 patients suffering from Non-Hodgkin Lymphoma and receiving CHOP combination therapy from November 2015 to April 2018 at Cancer Hospital Jamshoro, sampling technique used was purposive. The response on ADRs was recorded and these were verified by comparing against British National Formulary (2017) and Lexi Comp Drug Information Handbook (2015).

Results: Among 100 patients enrolled aged 18-65 years in which females comprise the majority. The common ADRs reported were nausea 71%, fatigue 69% and alopecia 68% The patients who responded about high severity ADRs also tend to stay longer as compared to those with less severity one.

Conclusion: The study results show that patients receiving lymphoma treatment suffers from high severity ADRs require supportive medical care as this lead to prolong effects after dose cycle. These patients must be counselled for supportive medication and food intake to prevent additional health risks to achieve maximum therapeutic benefits.

Keywords: Cancer, Anticancer Drugs, Chemotherapy, CHOP Therapy, ADRs

INTRODUCTION

Cancers that originate in lymphocytes within the lymphatic system are termed as Lymphomas. Most often these cancers first form in lymph nodes. On-Hodgkin lymphoma (NHL) is employed for a range of the cancer related to the blood that originate a single feature that they crop up from damage to the genetic material of a parent cells of lymphatic system which result in an exaggerated and uncontrolled growth of the lymphocyte.^{1,2,3,4,5,6,7} NHL usually develops in lymph nodes of stomach intestine or skin. Symptoms include Distended lymph node in areas like neck, armpit or groin, sometimes a swollen node adjacent to ears, elbow or in the throat close to the tonsils. Enlarged spleen, weight loss, loss of appetite, fever, fatigue, excessive sweating especially in night. cough, chest pain, bone pain, abdominal pain, rashes or kin lumps when disease originate in areas aside from lymph nodes such as lung, bone, skin or gastrointestinal tract. NHL diagnosis involves a lymph node biopsy which is also termed as immunophenotyping and cytogenetic analysis which also helps in identifying the subtypes. Blood tests are performed to investigate for blood diseases and indication of other diseases. Generally, chemotherapy and radiotherapy are two principal forms of the treatment for lymphoma. The clinical trials suggested various single and combination of chemotherapeutic agents for treatment of NHL. The drugs preferred include Carboplatin isplatin, cholrambucil, Cyclophosphamide, Doxorubicin, idrubicin, Cytrabne, fludarabine, gemcitabine, methotrexate, paclitaxel, etoposide, vincristine, vinblastine, dexamethasone, prednisone, rituximab etc.^{8,9,10,11} The combinations preferred for treatment of NHL include: CHOP (Cyclophosphamide, doxorubicin, vincristine, prednisone). R-CHOP (prednisone +rituximab, +doxorubicin,+ Cyclophosphamide, +vincristine) R-or F-CVP (rituximab or Fludarabine,+ Cyclophosphamide, vincristine, prednisone), ICE (Ifosamide, carboplatin, etoposide), R-HCVAD (rituximab, Cyclophosphamide, vincristine, doxorubicin), DHAP (dexamethasone, high dose cytabine, cisplatin) Chemotherapy is associated with various types of ADRs as they possess cytotoxic nature prone to various unwanted effects. An evaluation of these effects can help in maintaining the quality of life of the patients.^{12,13,14,15}

MATERIALS AND METHODS

This was a prospective observational study. It was conducted by including 100 patients who were diagnosed with non-Hodgkin lymphoma. Those patients were prescribed CHOP combination chemotherapy for its treatment. Patients aged above 18 years of age receiving CHOP therapy were included in the study. The data was collected by purposive sampling technique from November 2015- April 2018 at cancer Hospital Jamshoro Pakistan. Approval with regard to ethics was obtained from Hospital, the research was conducted as per the declaration of Helsinki and informed consent also obtained from participants included.

Demographic, diagnosis and therapy information of patients were obtained from their medication record file. The feed back of patients were recorded in a validated questionnaire. Data was analyzed by using SPSS (Statistical Package for Social Sciences) software version 22

RESULTS

CHOP combination therapy was found to be one of the common regimens for treating lymphoma especially non-Hodgkin lymphoma (NHL). The present study included 100 patients receiving a CHOP regimen with dose 750/50/1.4mg/m² day 1 and 100mg (prednisone) per oral day 1-5 repeated every 21 days and their response on ADRs recorded. Various ADRs reported by the patients include the following. Lymphoma (NHL) patients receiving CHOP therapy for the treatment, most frequent ADRs associated with the gastrointestinal tract were nausea, vomiting, acidity, and anorexia appeared among most frequently reported ADRs Table .1. Acidity and anorexia accounts for 71%, 64%, 64% and 53%, respectively. Other ADRs reported with comparatively less frequency include indigestion. The Majority of patients reported that these ADRs occur with a severity level of 3-5 according to the Hartwig and Siegel scale, and these persist for a duration of 3 days to a week. Those reported with a severity level of 1-2 or occasionally feeling such symptoms persist for day 1-2 after each chemotherapy cycle. Blood cell effects observed in the blood reports includes most common anemia 51%, leucopenia accounts for 37% whereas thrombocytopenia 35%. In all type of disorders majority were of high severity. Anemia found to be most common ADR with prevalence of 51%.

Table 1: Undesirable effects observed affecting various systems

Gastrointestinal System effects						
ADRS	Total (n/%)		Level 1-2 (n/%)		Level 3-5 (n/%)	
Nausea	71	71	21	21	50	50
Vomiting	64	64	14	14	50	50
Anorexia	53	53	15	15	38	38
Acidity	64	64	16	16	48	48
Indigestion	40	40	16	16	24	24
Abdominal Pain	39	39	21	21	18	18
Diarrhea	20	20	15	15	5	5
Constipation	10	10	4	4	6	6
Mucositis	36	36	13	13	23	23
Cardiac Effects						
Tachycardia	36	36	10	10	26	26
Bradycardia	12	12	12	12		
Blood Components effects						
Leucopenia	37	37	14	14	23	23
Thrombocytopenia	35	35	13	13	22	22
Anemia	51	51	13	13	38	38
Neurological and other effects						
Fatigue	69	69	19	19	50	50
Insomnia	61	61	10	10	51	51
Vertigo	61	61	13	13	48	48
Numbness	50	50	15	15	35	35
Tinnitus	37	37	13	13	24	24
Amnesia	59	59	59	59		
Hearing Disturbances	15	15	15	15		
Vision Disturbances	20	20	20	20		
Alopecia	68	68	12	12	56	56
Skin problems	10	10	10	10		
Fever	12	12	12	12		

Tachycardia was reported by 36% of the patients and bradycardia by 12% of patients. Neurological and others include Fatigue, alopecia, insomnia vertigo, and amnesia the most commonly reported ADRs that result in affecting the activities of daily life. These lead to huge distress and discomfort as a majority of them reported as high severity ADRs. Other ADRs reported with less frequency include numbness, tinnitus, hearing disturbance, vision disturbance, skin problems. No, any patient-reported about having a fever as a result of chemotherapy administration. Figure 1,2,3 showing the graphical presentation of ADRs associated with CHOP therapy.

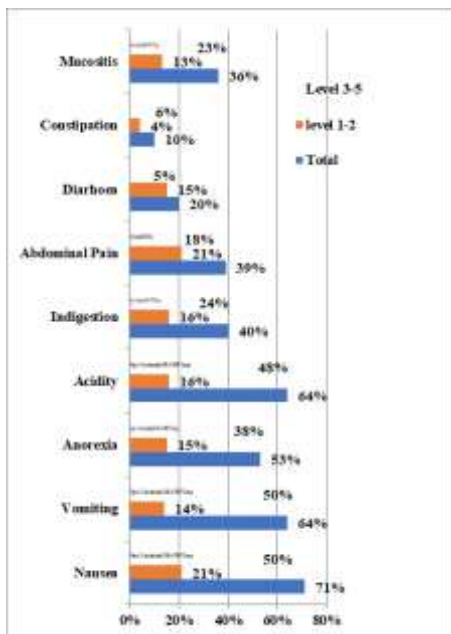


Figure 1: Gastrointestinal ADRs of CHOP Therapy

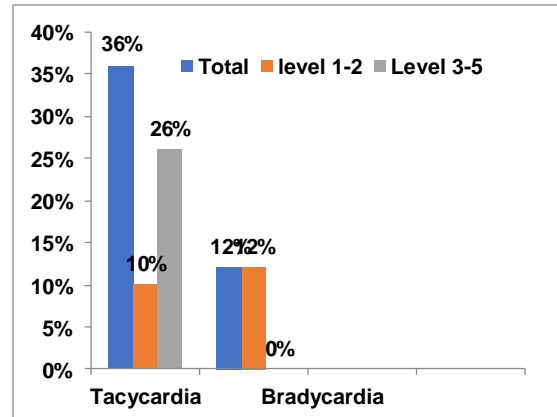


Figure 2: Cardiac disorders due to CHOP therapy

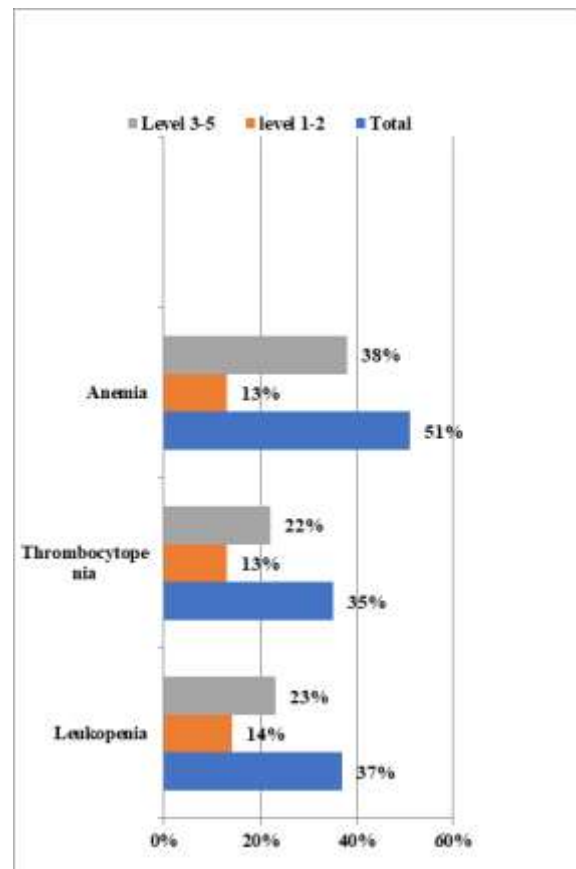


Figure 3: Blood disorders due to CHOP Therapy

vomiting was reported by 64% among which 50% reported

DISCUSSION

The treatment of lymphoma with CHOP combination therapy results in various ADRs in patients and most commonly reported were nausea, fatigue and alopecia. Sam anbu sahayam J et al (2016) study evaluated the adverse effects of CHOP therapy and results include out of 30 patients nausea/vomiting accounts for 53.3% patients in this study subjects it was 64% one of the common ADR reported. ¹⁶ Bertrand C offier , m.d., Eric I epage , M.D., P h .d.et al, 2002) study presented the non hematologic ADRs of chop include nausea or vomiting 48% and 8%, nausea in

present study subjects was most common ADR accounts for 71% among which 50% reported with high severity level whereas it with high severity level. Sam anbu sahayam J et al (2016) Mucositis 31% and 2% in this study subjects it was 36% and 23% of high severity level, Bertrand C offier, m.d., Eric Lepage, M.D., Ph.D. et al, (2002) it was 30%.¹⁷ Celsing F et al (1998) wrote stomatitis /mucositis was reported by 20% and 2%, in this study 13% patients reported it with low severity level whereas 23% patients reported it with high severity level. Diarrhea reported with low severity grade by 20% and high severity grade by 4%, similarly in this study it was reported by 20% patients among which 5% reported it with high severity while 15% reported it with low severity ADR. Anemia found to be common blood disorder in their study accounts for 20%, in this study subjects it was also common one accounts for 51%, whereas leucopenia with prevalence of 16.67%, which in this study subjects was 37%.¹⁵ study results found reduction in WBC count was most commonly reported ADR with frequency of 9% of 1-2 grade and 87% of grade 3-4. Anemia in their study was observed in 57% with low severity grade while in 19% high severity grade. Reduction in platelets was which in their study it was 24% and 17% with low and high grade severity ADRs respectively.¹⁵ Sam anbu sahayam J et al (2016) study Tingling and numbness 20% in their study which in this study reported by 50% patients. Alopecia in current study was one of the most common ADR reported by 68% patients according to their study it was 23.3%.¹⁶ Bertrand C offier, m.d., Eric Lepage, M.D., Ph.D. et al, (2002) Alopecia appeared most common in their study with frequency of 97% and 45%. In this study Constipation was least commonly reported by study subjects with frequency 10% and among which 6% reported it with high severity. But in Bertrand C offier, m.d., Eric Lepage, M.D., Ph.D. et al, (2002) 's study it appeared more common in their study with prevalence of 41% and 5%, whereas as Cardiotoxicity 35% and 8% in this study it was reported as tachycardia and bradycardia symptoms with a frequency of 26% and 10% of high severity level and 12% respectively. Fever was reported one of the most common ADR in their study with frequency of 59% and 5% with high grade, which in current study it was 12% but with less severity¹⁷.

CONCLUSION

The study results show that Combination chemotherapy of CHOP can affect patient's life style if caused high severity ADRs. must be counselled for supportive medication and food intake to prevent additional health risks to achieve maximum therapeutic benefits.

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