

A Phase II Study of Doxorubicin, Vincristine, Cyclophosphamide, Prednisolone (CHOP) Chemotherapy with Intrathecal (IT) Methotrexate and Prophylactic Cranial Irradiation in a Patients with High Grade Non Hodgkin's Lymphoma (NHL)

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Objective: The objective of this phase II study was to evaluate the efficacy and toxicity of (CHOP) chemotherapy with intrathecal methotrexate and prophylactic cranial irradiation in patients with high-grade Non Hodgkin's lymphoma. **Method:** From January 2002 to December 2002 twenty consecutive patients with histopathologically and immunohistochemically confirmed high grade NHL with Ann Arbor stage III & IV were enrolled. ECOG performance status of 0 or 1 was required. Written informed consent was obtained from all patients. Patients with symptomatic meningeal or brain involvement were excluded from the study. Cyclophosphamide 750 mg /m², vincristine 1.4 mg / m² (maximum 2 mg), doxorubicin 50 mg / m² was given I/V on D1 and prednisolone 100 mg PO was given from D1 – D5. Cycles were repeated after every 21 days. Intrathecal methotrexate was given at a dose of 12 mg once during 3rd week, twice weekly on 5th & 6th week and once during 7th week. A total dose of 1800 cGy was given to whole brain in 10 fractions with a daily tumor dose of 180 cGy using a Cobalt 60. Common Toxicity Criteria was used for evaluation of toxicity and WHO criteria for response evaluation. **Result:** All 20 patients were able to complete the planned therapy. Grade IV neutropenia was observed in 45% (9/20) of patients. Episodes of febrile neutropenia were seen in 20%(4/20). Grade II diarrhea was seen in 25%(05/20). 20%(4/20) had grade II cutaneous toxicity. No immediate radiation related toxicity was seen except grade II nausea and vomiting. Overall response was found in 75%(15/20) of patients, CR in 60%(12/20) and PR in 15%(03/20). 15%(03/20) patients showed stable disease and 10%(02/20) had progressive disease. **Conclusion:** This combined modality treatment of CHOP chemotherapy with intrathecal methotrexate and prophylactic cranial irradiation has been feasible and effective with acceptable toxicity in this group of patients with high-grade Non Hodgkin's lymphoma.

Key words: High grade non-hodgkin lymphoma, cranial radiation, intrathecal

Non-Hodgkin's lymphoma (NHL) accounts for 4 - 5% of new cancer each year and is responsible for 5% of deaths with cancer in the United States. It was estimated for the year 2000, that there will be 54,900 new cases of NHL diagnosed in the United States, and that 26,100 people will die with this diagnosis. No such data exist for Pakistan however it is seen as the 4th common tumor in some of reports in country¹.

Currently "REAL" classification is used to classify NHL and it includes immunoblastic lymphoma, lymphoblastic lymphoma, Diffuse, small non-cleaved cell lymphomas². Lymphoblastic and immunoblastic lymphoma account for 30 - 40% of childhood NHL and share many clinical and biologic features with ALL and are treated as ALL³. The survival rates of 85-90% have been achieved with different combination chemotherapies without significant mortality and morbidity as reported by several single institution and co-operative groups⁴.

Early preventive CNS therapy is critical in the treatment of advanced stage lymphoblastic lymphoma. IT chemotherapy alone or combined with cranial irradiation has been mainstay of CNS preventive therapy.⁵ Patient's with (early stage) had sustained remission with single or multiple dose cyclophosphamide where as majority of patient's with advanced tumor relapsed with systemic and

CNS disease. Because of the propensity for CNS metastasis, treatment regimens for Burkitt's lymphoma always involve prophylactic therapy to CNS⁶.

CHOP is used as a first line therapy in patients with high-grade Non Hodgkin's lymphoma in Pakistan at most of the centers but the intrathecal chemotherapy and prophylactic irradiation is not being used routinely. High dose chemotherapy with stem cell transplant, which is now a new treatment option of high grade NHL is not being practiced in most of our centers in Pakistan because it is very toxic and difficult to manage, therefore there is a need to improve the treatment of high grade NHL so the existing therapeutic modalities should be integrated and also the benefits of CHOP and CNS prophylactic therapy are not fully explored.

Primary objective:

To study the safety and feasibility of combination of CHOP chemotherapy, intrathecal methotrexate and prophylactic cranial irradiation

Secondary objective:

To determine the effectiveness of this combined modality treatment in preventing CNS relapse in patients with high grade NHL. To document the response rate.

