

Clinical Outcome of Management of Acute Myeloid Leukemia with Idarubicin plus Cytarabine

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A prospective study was conducted at Department of Clinical Oncology, King Edward Medical College / Mayo Hospital, Lahore from July 2003 to June 2004 to evaluate the effect of Idarubicin plus Cytarabine in chemo naïve Acute Myeloid Leukemia (AML) patients. A total of 15 consecutive patients were enrolled with age group 15-58 years. Patients were classified according to French American British (FAB) classification. Induction therapy with Cytarabine as continuous infusion for 7 days and Idarubicin was given on day 1-3. For assessment of response, all patients were subjected to bone marrow examination fifteen days after completion of Induction chemotherapy. Consolidation Therapy with high dose Cytarabine was given on days 1, 3 and 5. Cytarabine was repeated after 28 days for 4 cycles in patients with complete remission after induction therapy. A remission induction rate of 66.7% was observed. Four patients died because of complications. One patient lost to follow up. Idarubicin and cytarabine is effective regimen for achieving complete remission in AML Chemo-naïve patients.

Key Words : Cytarabine, AML, Idarubicin.

Acute Myeloid Leukemia is a clonal disorder characterized by the proliferation of abnormal blast cells and impaired production of normal blood cells¹. The incidence of AML in USA is 3/100 000 persons². Acute leukemia represents almost 5% of all new cancer cases but among persons younger than thirty-five years, acute leukemia is the most common cause of cancer death³. For AML, incidence increases steeply beyond the age of 50, with median age being 60 years^{4, 5, 6}. Ionization Radiations and Benzenes are clearly associated with increased risk of acute leukemia and this leukaemia has poor prognosis. Same is true for alkylating agents and Topoisomerase inhibitors such as Etoposide and anthracyclines⁷. Treatment related leukemia is associated with poor prognosis and allogenic transplantation in first remission should be considered in these cases. AML secondary to NHL have worst prognosis⁸. AML occurs more commonly in the family members than would be expected by chance. Siblings have approximately two fold increased risk of AML. Infectious agents are not related with AML except for Human T-lymphocyte Leukemia Virus-I (HTLV-I) related leukemia. Congenital disorders like Down's syndrome, Fanconi's Anemia, Bloom's syndrome and Ataxia Telangectasia are also associated with increased incidence of AML³.

Methodology:

From July 2003 to June 2004, 15 consecutive chemo naïve AML patients were enrolled with age group 15-58 years. Patients were classified according to FAB classification. Pre chemotherapy work up included CBC, blood urea, serum creatinine, Serum uric acid, PT, APTT, FDPs, fibrinogen, LDH, Urine analysis, chest X-Ray PA view, ECG, Echocardiography and ultrasound abdomen. All 15 patients received Induction chemotherapy with Cytarabine

150-200 mg/m² continuous infusion for 7 days plus Idarubicin 12 mg/m² IV push on day 1-3 (All Trans Retinoic Acid could not be given to patients with AML M3 because of non availability of this drug). All patients were subjected to Bone marrow examination 15 days after completion of Induction. Consolidation chemotherapy with Cytarabine 6 gm/m² 24 hours infusion (3gm/m² bid) on days 1, 3 & 5 was given and repeated after 28 days for 4 cycles in patients having complete remission after induction chemotherapy.

Results:

Patients characteristics regarding age, sex, performance status and complications are given in table 1 and types of AML at presentation are given in table 2. Ten out of 15 patients achieved complete remission (66.7%). Two patients (13.3%) died because of infection during induction therapy, two (13.3%) died due to neutropenia and one (6.6%) lost to follow up.

Table 1: Patients characteristics (n=15)

Characters	n=
Sex	
Male	10
Female	02
Average age	
Male	44 years
Female	37.8 years
Performance status	
ECOG 1	5(33.3%)
ECOG 2	10(66.7%)
Complications	
Infection	11(73.3%)
Haemorrhage	3(20%)
Neutropenia	15(100%)
Thrombocytopenia	15(100%)

Table 2: Types of Acute Myeloid Leukemia at presentation (n=15)

Type of AML	Total Patients	Percentage
M1	2	13.3
M2	5	35.3
M3	3	20
M4	3	20
M5	1	6.7
M6	1	6.7

Discussion:

In this study, overall remission rate was 66.7% i.e. 10 out of 15 patients achieved complete remission. Wiernik et al (1992)⁹ showed complete response rate of 70% with Idarubicin + Cytarabine as induction therapy for AML. The complete remission rate in patients age between 18-50 years was significant i.e., 88%. In another study by Baser et al (1993)¹⁰, complete remission rate was 90% for those aged < 60 years. Dinndorf et al (1997)¹¹ observed remission rate of 80%.

Complications in different patients vary. Neutropenia and thrombocytopenia was observed in 100% of patients with induction therapy. Infection in 73.3% and 03 patients (20%) showed haemorrhage. William et al (2002)¹² reported that neutropenia occurs frequently in AML patients undergoing induction therapy with idarubicine and cytosine. In a large southeastern cancer study group trial¹³, 57% of patients undergoing induction therapy with idarubicine developed grade I – II and 16% Grade III – IV neutropenic colitis (diarrhea).

Conclusion:

The idarubicine and cytarabine combination induction chemotherapy is effective regimen for AML Chemo-naïve patients.

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