RESEARCH COMMUNICATION

Control of Acute Myeloid Leukemia Morbidity in Northwest Iran

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Abstract

Background: To investigate protocols of remission induction therapy for prevention of morbidity of acute myeloid leukemia. Materials and Methods: The responses of 150 patients to "2+5" and "3+7" protocols during 1996-2003 were assessed and analyzed with the Chi- Square method. Results: Complete remission was observed in 30% of cases treated with 2 days of daunorubicin and 5 days of cytarabine (2+5 regimen). Remission was increased to 52.5% when patients were treated with 3+7 regimens with the same drugs. Partial remission resulted in 25 and 10 percent of cases, respectively. Conclusion: As in previous studies the 3+7 regimen was demonstrated to be more effective than the 2+5 regimen in our hospital (p=0.0009).

Key Words: Remission - induction therapy - acute myelogenous leukemia

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Introduction

Acute leukemia is classified broadly as either acute myelogenous leukemia (AML) or acute lymphoblastic leukemia (ALL), with a 30% blast threshold in marrow traditionally used to separate the two. The proposal by the WHO working group to lower this threshold to 20% has stirred controversy (Head, 2005). The main treatments include remission induction therapy and post-remission chemotherapy (Kimura, 2003). The use of anthracyclines and cytosine arabinoside (ARA-C) in different combinations significantly increases the rate of remissions (Gross et al., 1982) and up to 40% of the patients are remained in continuous remission longer than 3 years (Meuret, 1983), but care needs to be taken regarding optimal dosages and schedules of administration (Stein, 1989). To assess effectiveness we here compared two protocols.

Materials and Methods

A retrospective study was conducted from 1996-2003 in our centre for determining the response rate of AML patients to different drug regimens. Two hundred and fifty patients with AML, aged13-60 years, were involved in this study where 50 patients received no chemotherapy, some of which died of sepsis and bleeding and some others were discharged due to status of low performance. Forty patients received the 2+5 protocol (ARA-C: 100 mg/m2 for 24 hr infusion for 5 days plus DNR: 45 mg/m2 for 2 days) and 160 patients received the 3+7 protocol (the same drugs with the same dosages for 7 and 3 days respectively). They received the same antibiotics and blood derivatives as needed and bone marrow aspiration was conducted 14 days after initiation of chemotherapy. Cytogenetic data were not available, but immunophenotyping was performed for some patients. AML was diagnosed by studying peripheral blood smears, bone marrow aspiration, and biopsy slides stained with Wright & PAS and Sudan black. All slides were independently reviewed by two colleagues not involved in the study. AML was defined as the presence of more than 30% of myeloblasts in the bone marrow and complete remissionwas defined as the absence of abnormal clinical symptoms and having less than 5% of myeloblasts in the bone marrow 14 days post-chemotherapy initiation. Partial remission was defined as 5-30% of myeloblasts in bone marrow. Patients who did not respond to treatment were defined as non-responsive. Subtypes of AML were determined accordink-to FAB classification. Promyelocytic leukemias received trans-retinoic acid in addition to chemotherapy regimen. Patients who could not receive complete drug regimen were excluded from the study. The results were analyzed with the Chi-Square method.

Results

Out of 250 patients, 134 were females and 116 were males. The median age was 35 years. They were from East Azerbaijan (70%), West Azerbaijan (20%), Kurdestan (5.2%), Ardabil (4%) and Zanjan provinces (0.8%). Subgroups of AML were: M0(0%), M1(8.8%), M2(45.6%),

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M3(24%), M4(12.8%), M5(2.4%), M6(4.8%) and M7(1.6%). In the 200 patients who received chemotherapy, 30% complete and 25% partial remission was observed in patients undergoing the 2+5 protocol with 45% of non-responsive. Complete and partial remissions were shown to be 52.5% and 10% among patients receiving the 3+7 protocol, with 37.5% non-responsive (p=0.0009). Seven of 10 patients in partial remission who were treated by the 2+5 protocol achieved complete remission after another treatment with the 3+7 protocol.

Discussion

Our results clearly indicate that the '3+7' protocol is after superior '2+5' protocol with the same drugs, in line with earlier findings (Rai KR. et al, 1981). Patient age and pretreatment Karnofsky score are considered the most useful predictors of treatment outcome (Schwartz et al,.1984) and leukaemias showing evidence of cytoplasmic maturation along the granulocyte and monocyte lines, as evidenced by granules, Auer rods, a high percentage of Sudan black positive blast cells and morphological and cytochemical abnormalities of neutrophils are associated with a higher rate of remission (Swirsky et al, 1986). Patients with leukocyte counts of less than or equal to 10,000/mm^3 at diagnosis or less than or equal to 40,000/mm^3 at the start of therapy, and those who received greater than 120 mg/m^2 of DNR demonstrate significantly longer remission and survival (Schwartz RS. et al 1984). We could not determine variation in leukocyte counts, but total dosage of DNR was 135 mg/m^2 in all patients.

In one earlier study about two thirds of patients achieved remission with a standard chemotherapy protocol (Suri et al 1990). Our remission rate in 3+7 protocol was lower, at 52.5%, but is comparable to the 55.3% rate reported by Nowrousian et al (1983). In another study, 51 patients (mean age 40, range 17-71) with previously untreated AML (25% of M4-6 FAB type) were given Ara-C subcutaneous 100 mg/m^2 every 12 h for 7 days and DNR 45 mg/m^2 on days 1-3 intravenously for inducing remission. After 52 days, 49% of patients on average reached CR (Holowiecki et al 1983). Intensive induction results in a higher cure rate, since reduction of blasts in bone marrow at 2 weeks after the initiation of therapy to less than 20% was found to be the most significant prognostic factor to predict long complete remission. (Ohno R, 1989). Idarubicin may be more cost-effective than DNR in the treatment of adult acute myeloid leukemia. A lower remission rate in DNR-treated patients, and thus their need for additional care, will increase the cost differences between the two treatments (Pashko, 1991).

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