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APOPTOSIS AS A THERAPEUTIC STRATEGY FOR ACUTE LYMPHOBLASTIC LEUKEMIA

IBRAHIM O.M.*, EL-ASHMAWY N.E.**, SIDHOM I.A.***, EL-KHODARY N.M. *

*Departments of *Clinical Pharmacy & **Biochemistry, Faculty of Pharmacy, Tanta University and ***Pediatric Oncology, National Cancer Institute, Cairo University, Egypt*

Abstract:

Objective : Defects in programmed cell death not only contribute to the development of cancer, but also influence the ability to treat it. This study was conducted to evaluate the role of chemotherapeutic drug combination in modulating the apoptotic pathway in children with acute lymphoblastic leukemia (ALL).

Patients and Methods: Forty newly diagnosed acute ALL patients below the age of 18 years were included in the study in addition to twenty healthy subjects, with matched age and sex, who served as control group. Patients were treated with induction therapy according to a special protocol over one month. The chemotherapeutic drug combination consisted of dexamethasone, vincristine, doxorubicin, L-asparaginase, etoposide and cytosine arabinoside (Ara-C). Beside diagnostic and prognostic laboratory investigations, peripheral blood lymphocytes were collected at the time of diagnosis and at remission, and were examined for the apoptotic index and DNA fragmentation. Serum was used for determination of caspase-3 activity (apoptotic enhancer) and Bcl-2 (apoptotic suppressor).

Results: Results indicated that apoptotic pathway was impaired in ALL patients as manifested by significant decrease in the apoptotic index and DNA fragmentation, but a significant increase in Bcl-2, compared to control group. Treatment of ALL patients with induction therapy enhanced the rate of apoptosis. Bcl-2 was significantly reduced, whereas caspase-3 activity and apoptotic index were significantly increased at the time of remission, compared to pretreatment levels.

Conclusion: Enhancing apoptosis can be a target for ALL chemotherapy, and the development of apoptotic enhancers may help control of hematologic malignancy.

Keywords: Acute lymphoblastic leukemia, chemotherapy, apoptosis, caspase-3, Bcl-2.