MINI-REVIEW

Risk Factors and Primary Prevention of Acute Leukemia

Gul Ilhan, Sema Karakus, Neslihan Andic

Abstract

Although risk factors for leukemia have been invastigated in numerous studies, only a few of them explain the disease etiology. Established and suspected risk factors for leukemia can be classified as familial, genetic , environmental (benzene, high dose ionizing radiation, chemotherapeutics, electromagnetic fields) and lifestyle (smoking, obesity, dietary intake). Prevention of leukemia may be possible by avoiding exposure to risk factors associated with leukemia such as smoking, benzene exposure and high dose ionizing radiation. To explain the etiology of all leukemias and develop preventive methods for the disease, future studies are needed.

Key Words: Leukemia - risk - prevention

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Introduction

Leukemias are hematological malignancies which have different subtypes as acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML) and chronic myeloid leukemia (CML). According to the American Cancer Society, approximately 35,070 individuals will be diagnosed with leukemia and leukemias will be responsible for 22,280 deaths (4% of all deaths for men and women) during 2006 in the United States. Since 1991, death rates in males and females have decreased by nearly 0.6% per year. Although causes of most of leukemias are not known, now with current studies, we have some evidence about risk factors. Our article reviews currently known risk factors and primary prevention of leukemia.

The established and suspected risk factors for leukemia can be classified as familial and genetic, life style and environmental types.

Familial factors

Genetic plays an important role only for a small proportion of cases (Kasim et al., 2005). There are some identified chromosomal anomalies related to leukemia. For example CML is found an association with the Philadelphia chromosome (usually translocation 9/22) (Greaves, 1997). The Down syndrome, Klinefelter syndrome, ataxia telangiectasia, Bloom syndrome and Fanconi anemia are chromosomal syndromes causing predisposition to leukemia (Robinson, 1992; Stiller et al., 1994). In the largest population-based study evidence for a strong familial clustering for multiple myeloma, CLL, non-Hodgkins lymphoma (NHL) was provided (Altieri et al., 2006). In another large population based study a remarkable familial clustering for NHL was apparent with few differences for various histopathologic subtypes (Altieri et al., 2005).

Lifestyle related risk factors

Smoking, obesity and diatery intake are lifestyle risk factors for development of leukemia. Cigarettea contains some leukemia-causing agents such as benzene and epidemiological studies have shown slight risk elevation for leukemia especially of myeloid type in smokers (Siegel, 1993; Friedman, 1993). In a large case control study, associations between smoking and acute leukemia were seen particularly in elderly patients (Sandler et al., 1993). In a Norwegian study a causal but weak relation between myeloid leukemia and smoking was noted (Engeland et al., 1997). In addition, the International Agency for Research and Cancer (IARC, 2004) and Surgeon General's reports (Carmona et al., 2004) concluded that there was causal association between active smoking and AML. In a large population based case control study designed in Canada for investigation of lifestyle factors for risk of leukemia, significant association was again seen (Kasim et al., 2005). However, in some studies an adverse association between smoking and CLL, ALL and hairy cell leukemia (HCL) was observed (Stagnaro et. al., 2001; Clavel et al., 1995).

Obesity is one of the risk factors. Although the mechanism is not known clearly, decrease of immune response with obesity (Marti et al. 2001; Chandra, 1997) and high plasma leptin levels may play roles in the etiology (Considine et al., 1995). In experimental studies with animals it was found that this hormone increased proliferation of CD4+ T cells and stimulated myelocytic and primitive hematopoietic progenitor cells (Umemoto et al., 1997).

Department of Hematology, Baskent University Medical School, Ankara, Turkey For Correspondence: gullhan2002@yahoo.com

Howeverm in a case control study interestingly it was seen that the risk of AML related to smoking to be reduced substantially in subjects with high BMI (≥30 kg/m2). This result was explained with active smokers were thinner than non-smokers. In two studies had small samples and lack adequate control of important confounding factors, it was found that high amount of vegetable taking reduced risk for AML (Kwiatkowski et al., 1993; Ross et al., 2002). In a case control study for some leukemia subtypes, risk was observed to increase with high or low fruit consumption (Kasim et al., 2005).

Environmental risk factors

These factors include benzene exposure, high dose ionizing radiation, chemotherapeutic agents and exposure to electromagnetic fields.

Benzen is a solvent that has been used for leather, printing and petrochemical industries and for production of a wide variety of agents (Wallace, 1989). Benzene exposure occurs at the workplace or by environmental sources such as tobacco smoking. Association with excess of leukemia incidence, mortality especially for AML has been recognized for several decades (Brandt, 1992; IARC 1982). In an epidemiological study performed among 28 500 shoe, slipper an handbag workers in Istanbul, 31 leukemic individuals were detected among this group of workers from 1967-1974. The crude incidence of leukemia in these shoe workers was 13.59/100 000 which is significantly higher than the leukemia incidence of 4/100 000 in the general population in Istanbul (Yaris et al., 2004). In other case control studies (Linos et al., 1980; Girard and Rivol, 1970) and cohort investigations (Ott at al., 1978; Rinsky et al., 1981; Infate et al., 1977) benzene related leukemia, particularly AML, was reported. In a case control study in China, long term benzen exposure (≥15 years) was observed to increase the risk of leukemia (Adegoke et al., 2003).

Ionizing radiation has been found as a risk factor for AML, ALL, and CML but not for CLL. In the Life Span Study (LSS), Pierce et al. evaluated atom bomb survivors from 1950 to 1990. Among the 86,572 persons studied 249 leukemia deaths were attributable to radiation exposure. Preston et al. found % 50 of all leukemias were attributable to radiation between 1950-1987 in Hiroshima and Nagasaki (Preston et al., 1994). Although high dose radiation exposure increases leukemia rates, low dose of radiation has limited role in the etiology of leukemia (Zeeb and Blettner, 1998).

Chemotherapy and leukemia association has been observed since 1970's. Especially alkylating agents cause significant increases the risk of leukemia. In patients treated for various malignancies elevation in likelihood of disease development was 10-100 fold (Boffetta and Kaldor, 1994). With increase of dose, frequency of courses, number of drugs and period of time, the risk of leukemia increases (Kaldor et al., 1992).

Electromagnetic fields (EMF) are areas of energy that surround any electrical device and produced by power lines, electrical wiring and appliances. Because magnetic fields which is a component of EMF can penetrate the body, EMF has been studied in relation to leukemia. In 1979, an association between household wiring codes and childhood leukemia was reported (Wertheimer and Leeper, 1979). However, there are only a few large studies investigating the association magnetic fields in home and leukemia in the long term and no consistent association has been observed. In a review on occupational exposure to EMF and adult leukemia, the hypothesis of positive association was supported to some extent but inconsistencies between studies prevented firm conclusions (Feychting, 1996). In the UK a mortailty study of electricity generation and transmission workers did not show any association between occupational exposure to EMF and the risk of leukemia (Harrington et al., 2001). However, in another study by Minder and Pfluger, an association was apparent (Minder and Pfluger, 2001). In a interview based case control study about occupational risk factors for leukemia in Shanghai, it was reported that EMF exposure increased the risk of CML (Adegoke et al., 2003).

Conclusions

There are familial and genetic, lifestyle-related and environmental risk factors regarding leukemia. Known familial and genetic factors predisposing to disease development are few. While smoking, obesity, dietary intakes, exposure to EMF have weak associations with leukemia, benzene, high dose ionizing radiation and chemotherapeutics are more attirubutable risk factors. Leukemia prevention may be possible by avoiding these factors. Because only 15%-20% of leukemia cases can be explained with currently known risk factors, further studies are needed to find new modifying influences and provide clues to prevention methods.

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