Antioxidant status in children with malignancies

Thesis

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By

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Contents

List Abbreviations

AFP	**:**	Alpha-fetoprotein
AGE	**:**	Advanced glycation end products
ALE	**:**	Advanced lipo-oxidation end products
ALL	**:**	Acute lymphoblastic leukemia
AML	**:**	acute myeloid leukemia
CAT	**:**	Catalase
CNS	**:**	Central nervouse system
COX	**:**	Cyclo-oxygenase
EBV	**:**	Epstein-Barr virus
FAP	**:**	familial adenomatous polyposis
GPX	**:**	Glutathione peroxidase
HIV	**:**	Human immuno deficiency virus
HL	**:**	Hodgkin lymphoma
HTLV	**:**	Human T-cell lympho tropic virus
LOX	**:**	Lipoxgenase
MDA	**:**	Malondialdhyde
NHL	**:**	Non-Hodgkin Lymphoma
PUFA	**:**	Poly unsaturated fatty acids
RNS	**:**	Reactive nitrogen species
ROS	**:**	Reactive oxygen species
SAMe	**:**	SAdenosyl-L-methionine
SOD	**:**	Superoxide dismutase
WBCs	**:**	White blood cells

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Introduction

Acute leukemia is the most common form of childhood cancer and is the primary cause of cancer related mortality in children, the etiology of leukemia is poorly understood, and both genetic and environmental factors have been implicated.

A huge body of evidence from human and animal studies indicates altered metabolism in cancer ***(Ziegler et al., 2005)***.

Antioxidants allow aerobic organisms to withstand daily episodes of oxidative stress by counteracting the adverse effect of free radicals, which are produced by metabolic activities within the body, the levels of antioxidants not only provide protection against oxidation but also reflect their consumption during acute oxidative stress. Whenever antioxidant capacity is outflanked by oxidative stress, tissue lesion may occur ***(Pelicano et al., 2003).***

Antioxidants constitute a highly heterogeneous group they include low molecular weight substances either water (e.g. ascorbic acid) or lipid-soluble (e.g vitamin E), incorporated in the body through nutrition. In addition a number of endogenous metabolites (uric acid, lipids, albumin, bilirubin) possess antioxidant activities ***(Malliaraki et al., 2003).***

The sum of endogenous and food- derived antioxidants represents the total antioxidant capacity (TAC) of extra cellular fluids, which can be assessed by various methods .TAC integrates the cumulative effect of all antioxidants present in the plasma and body fluids and may give more relevant biological information as compared to the obtained by the measurements of individual parameters ***(Kampa et al., 2002).***

In vitro and in vivo data suggest that certain antioxidants selectively inhibit the growth of tumor cells, may induce cellular differentiation, and may alter the intracellular state, thereby enhancing the effects of cytotoxic therapy ***(Conklin, et al., 2002).***

Aim of the Study

The aim of the present study is to:

i. Identify antioxidant status in children with malignancies.

ii. Investigate the effect of conventional chemotherapy on antioxidant status.

iii. Determine the effect of antioxidant status on treatment related toxicities.

Pediatric Malignancies

1- Acute Lymphoblastic Leukemia:

Epidemiology:

Acute leukemia, the most common form of cancer in children, comprises approximately 30 percent of all childhood malignancies, with acute lymphoblastic leukemia (ALL) being five times more common than acute myeloid leukemia (AML). Each year in the United States approximately 2500 to 3500 new cases of ALL are diagnosed in children. Survival rates for leukemia have improved dramatically since the 1980s, with a current five-year survival rate of approximately 78 percent. This improvement is in large part because of treatment of large numbers of children with sequential standardized research protocols. Approximately 75 to 80 percent of children with newly diagnosed ALL participate in clinical research trials, the goals of which are to improve clinical outcome and to minimize acute toxicities and late-occurring adverse events ***(Greenlee et al., 2000).***

As mentioned above, approximately 2500 to 3500 new cases of ALL are diagnosed in children each year in the United States with an incidence of 2.8 cases per 100,000.It appears the incidence of childhood leukemia is increasing as demonstrated by the two following studies: In a study that used data from 63

European population-based cancer registries of children diagnosed with cancer, the incidence of leukemia including ALL increased by an average of 1.4 percent from 1970 to 1999. In a study from Great Britain, the incidence of leukemia (mostly attributable to ALL) has steadily increased from 3.83 to 4.61 per 100,000 persons by sex and age from the five-year period of 19971 to 1975 and 1996 to 2000 ***(Shah and Coleman, 2007).***

In contrast, a study from four Nordic countries (Denmark, Finland, Norway, and Sweden) reported that the incidence of childhood ALL remained stable at an approximate rate of 3.3 cases per 100,000 children below 15 years of age from 1983 to 2002 after an increase in incidence between 1975 and 1983.The peak incidence occurs between 2 and 5 years of age, and it occurs more commonly among boys than girls. In the United States, ALL occurs two times more commonly among white than black children ***(Svendsen et al., 2007).***

Diagnosis:

The diagnosis and classification of leukemia are based upon specialized tests that are performed on cells derived from a bone marrow aspirate or tissue biopsy specimens. When clinical circumstances preclude bone marrow examination, the diagnosis can be made from cells obtained from peripheral leukopheresis or pleural effusions. The diagnosis of CNS