A PROSPECTIVE STUDY TO EVALUATE HEMOSTATIC AND METABOLIC PROFILES IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA RECEIVING L-ASPARAGINASE

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List of abbreviations

ALL…… Acute lymphoblastic leukemia

ALT……Alanin transaminase

AML…….. Acute myeloid leukemia

ANLL…….. Acute non lymphoblastic leukemia

AST……..Aspartate transaminase

BFM……Berlin-Frankfort-Munster

C-ALL……Common ALL

CCG……Children's Cancer Group

CD……Cluster of differentiation

CNS……Central nervous system

CSF……Cerebrospinal fluid

D M……Diabetes mellitus

EcA……Escherichia coli Asparaginase

EPV……Epstein Bar Virus

FAB……French-American-British

HIV……Human immunodeficiency virus

L-ASP……L-asparaginase

MRD……Minimal residual disease

PEG-ASP……Polyethylene glycol asparaginase

PT……Prothrombin time

PTT……Partial thromboplastin time

TAT……Thrombin anti thrombin

TLC…….. Total leucocytic count

WBC……White blood cell

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Conclusion and recommendations

*****ALL induction therapy is a very critical period, with significant hemostatic & metabolic derangement.

*A significant increase in TAT complex was observed in the ALL patients especially in the high risk group.

*Since, increased TAT complex in plasma indicates in vivo thrombin generation so this complex seems to be a sensitive assay for early coagulation derangement in such patients.

*From these results, it is possible that hypercoagulability state exists in ALL patients during induction therapy.

*Significant hypertriglycedemia & increased serum amylase level were detected during & persistent after ALL induction therapy.

*Hyperglycemia was detected during induction therapy and regular follow up of blood glucose level is mandatory during induction therapy with L- asparaginase.

*Large studies are needed to determine the incidence of coagulation & lipid abnormalities in long –term survivors of ALL as well as the relation between such abnormalities & other late effects of treatment, like cerebrovascular & cardiac complications.

DISCUSSION

Acute lymphoblastic leukemia (ALL) is the most common malignancy of childhood ,representing nearly one third of all pediatric cancers. Chemotherapy treatment is associated with long list of side effects ,some common side effects are bone marrow suppression and immunosupression.

L-asparaginase as a single agent chemotherapy has yielded complete remission rate of 60% and hence it is considered one of the important induction drugs in ALL treatment(Sahu,1998).

The present study aimed to study hemostatic and metabolic changes at time of diagnosis of ALL, during and after induction therapy ,and to find out any possible association between such changes ,clinical presentation ,hematological parameters and ALL risk status .

This study comprised 30 patients with acute lymphoblastic leukemia below the age of 18 years, who

presented to the Pediatric Oncology Clinic,Childrens Hospital Ain Shams University and Tanta Cancer Center.

The median age of patients in the present study was 7 years with a mean of 7.35±3.97 years and a peak age incidence of 5-10 years which is in agreement with (Reiter et al, 1994).

Regarding the sex distribution, there was obvious male predominance ,male represents 61% of total patients with male : female ratio of 1.3: 1. This is in agreement with most series which reported a male: female ratio of 1.5:1 to 2.5:1 in ALL (Reiter et al,1994 , Margolin and Poplack ,1997).

Regarding FAB morphological classification L2 was the most common subtype in this study which represents 46.6% of the ALL patients .Similar findings was reported by (Pui et al ,2000). According to immunophenotyping the most frequent immunophenotyping encountered was the pre-B in 13 patients in (43.3%) followed by C-ALLA in 10 patients (33.3%), T-cell in 6 patients (20%) then early B in one

patient (3.3%) ,which is in agreement with (Kamel et al, 1996) .

In the current study lymphadenopathy was found in 63% ,hepatomegaly in 14% and splenomegaly in 46% of the patients. These results are in concordance with the Egyptian study by kosary, et al, 1999.

We studied the effect of asparaginase on coagulation and metabolism during induction therapy and we found that there was a small subgroup of children with elevated prothrombotic marker before we started the treatment. TAT level was significantly elevated in (7/30) patients prior to start of chemotherapy which indicate the disease it self can cause thromboembolic complications , There was statistically significant increase in the mean level of TAT during induction therapy and after remission induction in comparison with pretreatment levels (p1=0.0 , p2=0.0 respectively) this goes with that reported in other studies (Mieczyslow, et al ;2000).

TAT in plasma reflects the amount of thrombin formed in the blood vessels and so an increase in this complex suggests the activation of the coagulation cascade in the blood stream (latent clotting activation)

From these results , it is possible that hypercoagulability or damage to vessel walls, which activates the coagulation cascade in these cases

Thromboembolic events (TE) are serious complications of childhood ALL treatment ,that results in significant morbidity and mortality . These events are strongly associated with the administration of L-asparaginase. There have been many studies reporting TE and assessing the coagulopathy associated with treatment (Priest et al ,1982).

Several authors (Inge, et al,2006) had studied the influence of asparaginase therapy on the coagulation state and had shown that the disease process itself causes an increase in procoagulant activity and endothelial injury, as well as decrease in natural coagulation inhibitors.

Albert, 1999, Matthias, et al, 2003 found that sparaginase as a single agent significantly decreases plasma concentrations of almost all coagulation proteins and inhibitors measured compared with plasma levels at presentation .Combination chemotherapy with asparaginase decrease plasma concentration of most