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Levels of homocysteine, folic acid and vitamin B12 in patients with paediatric acute lymphoblastic leukaemia

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Dear Editor

Micronutrient deficiency including that of folate and vitamin B12 as well as hyperhomocysteinemia has been found to be associated with increased cancer risk by causing DNA damage due to single and double strand breaks and oxidative injury.¹ Therefore, this work was planned to determine the levels of Homocysteine (Hcy), folate and vitamin B12 in patients of acute lymphoblastic leukemia (ALL) at the time of diagnosis and after one month of induction chemotherapy.

This study was conducted on 30 diagnosed patients of ALL and 30 age and sex-matched healthy controls. Patients were monitored both clinically and haematologically (blood cell counts and bone marrow examination).

All the patients were given chemotherapy as per protocol (MCP841) regimen 1 consisting of prednisolone, vincristine, L-asparaginase, daunorubicin and intrathecal methotrexate. Remission criteria included: <5% blast cells in bone marrow and absence of leukaemic cells in blood, restoration of normal peripheral blood count and absence of physical findings attributable to leukaemia.

Venous blood sample was collected aseptically from the antecubital vein at the time of diagnosis i.e. before the start of chemotherapy and after four weeks of induction chemotherapy. Serum homocysteine (Hcy), vitamin B12 and folate were estimated by chemiluminescence technology using Advia Centaur CP (Siemens). A reference value of 3.7-13.9 $\mu\text{mol/L}$ for Hcy, 0-5.8 ng/mL for folate and 215-961 pg/mL for vitamin B12 was considered for comparison of test results.

The levels of Hcy, folate and vitamin B12 in controls and in ALL patients before and after chemotherapy are shown in Table 1. A positive correlation was found between levels of the serum Hcy and TLC ($r = 0.795$, $p < 0.001$) while a negative correlation was found between levels of the serum folic acid and TLC ($r = -0.596$, $p < 0.01$) and also between serum vitamin B12 levels and TLC ($r = -0.537$, $p < 0.01$) in ALL patients at the time of presentation.

Out of 30 patients, 28 patients achieved complete remission whereas two patients could not attain remission after four weeks of induction chemotherapy. The levels of Hcy, folate and vitamin B12 in ALL patients in remission and non-remission before and after chemotherapy are shown in Table 2.

Discussion

In the present study, there was significant increase in serum Hcy levels and a decrease in the serum levels of folate and vitamin B12 in ALL patients at the time of diagnosis. These may be due to intracellular redistribution of the folate pool in favour of malignant DNA synthesis, reduced capacity for remethylation of Hcy and a subsequent accumulation of Hcy in plasma.² After one month of induction therapy, we observed that the levels of Hcy were decreased and those of folate and vitamin B12 were increased. When malignant DNA synthesis ceased, remethylation of Hcy normalised and the plasma concentration of total Hcy dropped to normal values.² Hcy has also been reported to act as an early tumour marker for diagnosis, monitoring of treatment and for screening of recurrences in various cancers.² A variety of biochemical changes including folate deficiency, oxidative stress, aberrant DNA methylation and production of Hcy thiolactone have been found to be associated with hyperhomocysteinemia which may be responsible for carcinogenesis.³

Low folic acid levels have been implicated in higher risk for genetic instability and a variety of cancers.¹ A significant negative correlation between the levels of vitamin B12 and folate with TLC, observed in this study, implies their requirement and utilisation by actively dividing cells.



In the non-remission group, the levels of Hcy decreased while those of folate and vitamin B12 increased after induction chemotherapy but this change was found to be statistically non-significant, though this is a guarded report as this group consisted of only two patients in our study. Further robustly designed research is needed in this field to support these findings and to comment on their clinical implication.

Sincerely,

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Table 2: Comparison of Hcy, Folic acid and vitamin B12 in ALL patients in remission and non-remission group before and after induction chemotherapy

Parameters	Patients in remission N=28		Patients not in remission N=2	
	Before Chemotherapy (Mean±SD)	After Chemotherapy (Mean±SD)	Before Chemotherapy (Mean±SD)	After Chemotherapy (Mean±SD)
Homocysteine (µmol/L)	17.81±4.87	10.27±2.88*	24.73±1.23	23.41±1.53**
Folic acid (ng/mL)	4.76±1.31	6.09±0.98*	3.40±0.28	3.90±0.71**
Vitamin B ₁₂ (pg/mL)	315.00±122.95	351.75±92.95**	312.00±4.24	347.00±1.41**

Table 1: Comparison of Hcy, folic acid and vitamin B12 between ALL patients (before and after induction chemotherapy) and controls

Parameters	ALL patients N=30		Controls N=30 (Mean±SD)
	Before Chemotherapy (Mean±SD)	After Chemotherapy (Mean±SD)	
Homocysteine (µmol/L)	18.27±5.02*	11.11±3.67#	10.93±3.86
Folic acid (ng/mL)	4.67±1.13*	5.95±1.013#	7.79±1.70
Vitamin B ₁₂ (pg/mL)	314±118.64**	351.23±89.71##	368±82.68

* p value <0.001 as compared to controls

** p value <0.05 as compared to controls

p value <0.001 as compared to patients before chemotherapy

p value >0.05 as compared to patients before chemotherapy