CORRELATION OF LONG NON-CODING RNA HOTAIR EXPRESSION AND CD117(c kit) IN ACUTE MYELOID LEUKEMIA (AML)

Zeinab Ibrahim Mourad[(1)], Omar Mohammed Ghallab[(2)], Nermeen El dabah[(1)], Rehab Adel Ali[(1)]

Department of Clinical and Chemical Pathology[(1)], Department of Haematology[(2)], Faculty of Medicine , Alexandria University

Introduction

Acute myeloid leukemia is a form of hematopoietic progenitor cell cancer that causes an increase in the number of immature myeloid cells in the bone marrow In Egypt, leukemia accounts for 10% of all cancers, with AML accounting for 16.9%.AML becomes increasingly frequent as people age. The typical age of onset is roughly seventy years. Men are more likely than women to have AML. In the last decade, evidence of links between a variety of long non coding RNAs (lncRNAs) and leukemia pathophysiology has increased. LncRNAs are transcripts that are longer than 200 nucleotides and do not code for proteins. They play a role in cellular processes including gene regulation, as well as the carcinogenesis, growth, and prognosis of various tumors. HOTAIR is one of lncRNAs that plays a key role in the development of cancers such as acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and multiple myeloma. HOTAIR expression was found to be substantially higher in leukemic cell lines and primary AML blasts. Clinically, AML patients with a higher HOTAIR had a worse prognosis than those with a lower HOTAIR. Previous researches have investigated HOTAIR and c-kit receptor (CD117) expression independently and their effect on prognosis of AML patients. The c-kit proto-oncogene encodes CD117, a transmembrane protein receptor. In normal hematopoiesis, the c-kit receptor (CD117) and its ligand, stem cell factor, play an important role. It has been shown that when myeloid commitment occurs in leukemias, its expression extremely increases. The CD117 receptor tyrosine kinase is expressed on the cell surface of hematopoietic stem cells, and its signaling is required for cell survival, multiplication, and differentiation. In the great majority of AML patients, it is present. Furthermore, mutations in c-KIT have been found in a subgroup of CBF AML patients (inv(16)/t (16;16) and t (8;21)).

Aim of the work

Our study aimed to assess the correlation between long noncoding RNA HOTAIR and CD117 (c kit) expression in newly diagnosed AML patients. .

Patients and Methods

This study was conducted on 50 individuals and they were divided into 2 groups:

Group A: included Twenty-five (25) newly diagnosed AML patients of both sexes admitted to Alexandria Main University Hospital.

Group B: included Twenty-five (25) patients presented for bone marrow evaluation for non-malignant conditions. All patients in the study were subjected to full history taking, thorough clinical examination, complete blood count, bone marrow aspiration, RNA extraction and quantitative real time PCR for the long non coding RNA HOTAIR by specific primers, flowcytometry assessment for AML diagnosis and quantitative assessment of CD117(c kit) and conventional cytogenetic analysis. Informed consent was obtained from all subjects before the study after a detail briefing of the study purpose.

Results

Table (1) Comparison between the two AML groups and controls according to $2^{-\Delta\Delta ct}$ of HOTAIR

$2^{-\Delta\Delta ct}$ of HOTAIR	AML		Control (n = 23)	H	p
	Group1 (n = 6)	Group2 (n = 19)			
Min. – Max.	104.6 –418.2	0.01 –17.12	0.0 –10.87	15.441*	<0.001*
Mean ± SD.	215.8 ±124.1	3.46 ±5.03	2.12 ±2.80		
Median (IQR)	196.2(107.5–272.1)	0.32 (0.15 –5.33)	0.95 (0.32 –2.73)		
Sig. bet. groups	$p_1<0.001^*$, $p_2<0.001^*$, $p_3=0.921$				

•In the current study, cases were divided into two groups according to HOTAIR expression. “Group 1” included AML cases with $2^{-\Delta\Delta ct}$ of HOTAIR > 100, while “group 2” included AML cases with $2^{-\Delta\Delta ct}$ of HOTAIR < 100.We compared between the two AML groups and the control group according to $2^{-\Delta\Delta ct}$ of HOTAIR and a statistically significant difference was found between group 1 and group 2 AML ($p_1<0.001$), and between group 1 AML and the control group ($p_2<0.001$), no significant difference was found between group 2 AML and the control group ($p_3=0.921$). Comparison between the 3 studied groups showed a statistically significant difference. (p<0.001)

Table (2) Correlation between CD117 and $2^{-\Delta\Delta ct}$ of HOTAIR

$2^{-\Delta\Delta ct}$ of HOTAIR	N	CD117			
		Absolute		Percentage	
		r_s	p	r_s	p
AML group 2	19	0.047	0.847	0.077	0.753
AML group 1	6	0.429	0.397	0.429	0.397

•r_s: Spearman coefficient

•On studying the correlation between CD117 and $2^{-\Delta\Delta ct}$ of HOTAIR no statistically significant correlation was found.

Conclusion

From this study, we concluded that:

1. Expression of HOTAIR is upregulated in newly diagnosed adult AML patients and it can be used as a diagnostic marker in these patients.
2. HOTAIR expression is not associated with poor outcome or prognosis in AML patients in our study.
3. There was no significant correlation between lncRNA HOTAIR and CD117(c-kit) expression in acute myeloid leukemia.
4. There is a group of AML patients with very high HOTAIR expression which need further assessment with higher number of patients.