Role of micro RNA as a key epigenetic regulator in promoting nuclear reprogramming in adult Egyptian chronic myeloid leukemia patient

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INTRODUCTION

Chronic myeloid leukemia (CML) is a myeloproliferative myeloid neoplasm characterized by excessive increase of immature hematopoietic progenitor cells in the bone marrow and increase in the number of white blood cells in the peripheral blood.

MiR-125b is one of the miRNA family, it is transcribed from two loci located on chromosomes 11q23 (miR 125b-1) and 21q21 (miR 125b-2) and involved in various types of diseases including hematological and solid malignancies.

AIM

To assess the role of microRNA 125b in newly diagnosed CML patients and correlate its expression with treatment response and clinical outcome.

METHOD

In this prospective study involve 32 newly diagnosed adult CML patients from hematology unit and 32 healthy controls of matched age and sex. The patients were followed up for 6 months.

Measurement of micro RNA125b in CML patients before starting treatment and after 6 months of follow up by polymerase chain reaction (PCR) technique.

CONCLUSIONS

microRNA125b expression may play an important role in course of chronic myeloid leukemia ant the response to treatment.

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RESULTS

The median value of MicroRNA125b was higher in CML patient group Vs control group with statistically significance {40 (31 – 46) Vs 20 (17.5 – 24), p < 0.0001}. After 6 months of follow up, The post-treatment median value of MicroRNA125b was lower than pre-treatment level with statistically significance {28 (17.5 – 50) Vs 40 (31 – 46.5), p < 0.0002}

Table (1): Comparison between CML patient group before treatment and control group as regards Micro RNA 125b

variable	CML group (32)	control group (32)	mann-whitney u test
	median (iqr)	median (iqr)	P value
microRNA125 b	40 (31 – 46)	20 (17.5 – 24)	< 0.0001**

Table (2): MicroRNA125 b level before and 6 months after treatment:

variables	Pre-treatment level	Post-treatment level	wilcoxon's test
	Median (IQR)	Median (IQR)	P value
microRNA125 b	40 (31 – 46.5)	28 (17.5 – 50)	< 0.0002**

The Initial microRNA 125b median value in chronic phase CML patients was 37(29-42) while it was 78(73-85) in accelerated phase CML enrolled patients with statistically significant difference with (p<0.005).

CML patients achieved response to treatment showed lower initial and follow up after 6 months median level of micro RNA 125b than in those achieved warning and failure response with statistically significance {32.5 (29 – 41) Vs 18.5(12 – 24), 78 (73 – 85)Vs 72 (62 – 73), 44 (42 – 46) Vs 45 (39 – 56) , p value 0.001, 0.000} respectively.

Table (3): Comparison between chronic and accelerated phase CML patients as regard peripheral blasts and serial Micro RNA125b initial value and 6 months after treatment:

variables	CML phase		mann-whitney test	
	CP	AP		
	No. = 27	No. = 5	Test value	P-value
Peripheral blasts	2 (1 – 3)	13 (12 – 14)	-5.200	0.000
initial microRNA125 b	37 (29 – 42)	78 (73 – 85)	-5.207	0.000
Micro.RNA125 b 6 months	24 (13 – 28)	72 (62 – 73)	-5.030	0.000

Table (4): Correlation between initial and serial microRNA125b detected values and clinical outcome before and after treatment

	CML			Kruskal-wallis test	
	Response	Warning	Failure		
	No. = 18	No. = 9	No. = 5	Test value	P-value
MicroRNA125 b	32.5 (29 – 41)	78 (73 – 85)	44 (42 – 46)	13.021	0.001
Micro.RNA125 b 6 months	18.5(12 – 24)	72 (62 – 73)	45 (39 – 56)	23.127	0.000

By using ROC-curve analysis, MicroRNA125b cutoff point ≤41 in predicting the response to treatment with Area under curve 0.869, sensitivity 83.3% and specificity 78.57 % (p < 0.0001).

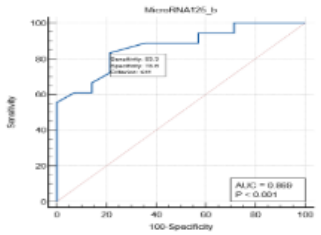

Figure (1): ROC curve of MicroRNA125 b (predicting the response to therapy).