Evaluation of MicroRNAs in Pediatric Epilepsy

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ICNC 2022
17th INTERNATIONAL CHILD NEUROLOGY CONGRESS
ANTALYA, TURKEY I OCTOBER 3-7, 2022

INTRODUCTION

Epilepsy is a chronic neurological disease and the incidence rates of epilepsy in childhood range from about 0.5 to 8 per 1000 person-years. The exact pathophysiology of epilepsy is still unclear. Neuron apoptosis may be closely associated with pathological circuit regeneration, inflammation, and glial fibroblast proliferation. MicroRNAs (miRNAs) may play a role in the genesis and development of epilepsy by regulating these pathological processes. miRNA are small non-coding RNAs and their main targets are messenger RNAs (miRNAs). Most previous research on the role of miRNAs in epilepsy has been done in adult patients. There are few studies on this subject with children. In this study, we aimed to evaluate microRNA expression in children with drug-resistant epilepsy and to compare seizure-free children with healthy controls with a single antiepileptic drug.

MATERIALS and METHOD

The study group included children with epilepsy followed by pediatric neurology. Healthy children and siblings of children with drug-resistant epilepsy were included in to control group. Only children with idiopathic generalized epilepsy who has normal brain magnetic resonance imaging were included in to study. Expressions of MiRNAs; miR-181a, miR-155, mir-146a, and miR-223 were searched.

RESULTS

The study was conducted with 43 patients and 66 controls. Sixty-five percent of (28/43) epilepsy patients were drug-resistant. Among healthy controls, 13 children were healthy siblings of epilepsy patients. The mean ages of epilepsy patients and controls were 113.41 ±61.83 (4-218) months and 105.46 ±62.31 (5-216) respectively. There was no significant difference between the mean ages of the groups ($p > 0.05$). miRNA expression analysis revealed an alteration of miR-155 and miR-223 in epilepsy patients compared to the controls (Table 1). In consideration of children with drug-resistant epilepsy, the same miRNAs were higher than controls ($p < 0.05$). The results showed that the expression miR-146a, miR-155 and miR-223 in drug-resistant epilepsy patients were higher than in drug-responsive ones (Table 2). There was no statistically significant difference in the expression of miRNAs between drug-resistant epilepsy patients and their healthy siblings ($p > 0.05$). The logistic regression analysis revealed that alteration of miR-155 was a risk positive factor for epilepsy whereas an alteration of miR-146a was a negative risk factor for epilepsy (Table 3). The results of logistic regression showed that also age does not affect miRNA expression ($p > 0.05$).

	Epilepsy patients	Controls	
MiRNAs	Fold Change Median $2^{-\Delta\Delta Ct}$ (min–max)	Fold Change Median $2^{-\Delta\Delta Ct}$ (min–max)	p-value
miR-146a	-0.99 (-4.88-2.18)	-0.43 (-5.88-10.21)	P > 0.05
miR-155	13.37 (10.33-16.08)	-4.18 (-14.25-17.28)	P < 0.05
miR-181	-0.60 (-3.55-15.31)	0.36 (-5.92-7.29)	P > 0.05
miR-223	3.29 (-0.40-6.99)	0.01 (-7.92-7.75)	P < 0.05

***Table 1**: miRNA 146a, 155, 181, 223 Expressions*

	Drug resistant patients	Drug responsive patients	
MiRNAs	Fold Change Median $2^{-\Delta\Delta Ct}$ (min–max)	Fold Change Median $2^{-\Delta\Delta Ct}$ (min–max)	p-value
miRNA-146a	-0.09 (-4.88-2.18)	-1.81 [(-2.76- (-0.02)]	P < 0.05
miRNA-155	13.72 (11.08-16.08)	12.15 (10.33-15.19)	P < 0.05
miRNA-181	-0.78 (-3.55-15.31)	2.16 (2.50-10.48)	P > 0.05
miRNA-223	3.61 (-0.40-6.99)	2.07 (-0.16-5.32)	P < 0.05

***Table 2:** Expression of miRNAs in drug resistant and drug responsive patients*

miRNAs	β	Standard error	P value	OR	%95 CI (min – max)
miR-181	0,030	0,086	0,727	1,031	0.87-1.221
miR-155	0,303	0,125	0,015	1,354	1.061-1.729
miR-146a	-0,635	0,295	0,031	0,530	0.297-0.945
miR-223	0,279	0,263	0,289	1,322	0.789-2.215

***Table 3:** Logistic regression analysis of expressions of miRNAs*

CONCLUSION

miRNAs represent 2-3% of the human genome and they are thought to regulate about 60% of the human genes. Increased miR1-46a levels in the epileptic brain may suppress inflammation. Our results showed upregulation of miR-146a decreases the risk of epilepsy and that miR-146a expression is significantly altered in drug-resistant patients. In conclusion, miRNAs 146a, 181a, 155, and 223, especially miR-155 and miR-223 may be involved in epilepsy pathogenesis. Expression levels of miRNAs might be useful to predict drug resistance.