LDL PARTICLE SIZE AND LIPID PROFILE IN CHILDREN WITH TYPE 1 DIABETES

Topuzovska S., Tosheska K., Labudovic D.
Department of Medical and Experimental Biochemistry, Faculty of Medicine, University “Ss. Cyril and Methodius”, Macedonia

The role of small dense low-density lipoprotein (sLDL) subclasses in atherosclerosis has been demonstrated in many studies. Among other metabolic changes, alteration in LDL lipoprotein subclass distribution and size has been proved in diabetic adults. Because there is not enough literature data presenting LDL subclass distribution in childhood, the aim of this study was to examine LDL subclass profile in diabetic children compared with healthy control.

Materials and Methods. In this study we evaluated 130 children, 30 children with type I diabetes mellitus and 100 controls, ages 9-18 years, matched for age, sex, and BMI.

Plasma LDL subclasses were analyzed using non-denaturing polyacrilamide gradient (3-31%) gel electrophoresis. Conventional plasma lipid and apoprotein parameters which are thought to affect LDL size were determined as well.

Results: The prevalence of small LDL particles (phenotype B) was in 86.7% of diabetic children, compared to control group (11%), with significant difference ($\chi^2=50.45; p<0.0001$). The smallest, LDL4 subclass was not found to be dominant in control children whereas in diabetic ones it was noted in 23%. Mean LDL particle size in diabetic children (24.64 ± 0.59 nm) was significantly smaller than in the control children (26.37± 0.68 nm; $p<0.0001$). The values for all measured conventional plasma lipid and apoprotein parameters in both groups were within the normal range for age of the children population. In diabetic children, LDL size was inversely correlated with plasma levels of triglycerides, and positively correlated with plasma HDL cholesterol and BMI. Overall, LDL size was not correlated with plasma concentrations of total cholesterol, LDL cholesterol, glucose, apoproteins and age in diabetic children. Although lipid and apoprotein plasma levels were within the normal range, increased frequency of LDL phenotype B confirms greater risk for atherosclerosis development in children with diabetes mellitus. LDL size measurement may potentially help to assess cardiovascular risk and adapt the treatment goals thereafter.

References:


The asymptomatic nature of esophageal cancer (EC) on early stage show the late clinical presentation leads to poor prognosis and limited success of therapeutic methods. Efforts to identify diagnostic/prognostic markers have been unsuccessful for clinics. Consequently, there is an urgent need for establishment of new non-invasive biomarkers for early diagnosis of EC [1]. The miRNAs are differentially expressed in normal and tumor cells of different subtypes of tumor tissues. Some miRNAs can be found in various biological fluids of the human body: blood, lymph, urine, etc. [2]. The level of circulating miRNAs can serve as an effective biomarker for early diagnosis of EC. The present study is aimed to identify miRNA binding sites in mRNA of genes involved in the development of EC and the clusters of miRNA binding sites in mRNA and their properties. Further, research of these miRNAs would provide a diagnostic strategy based on prevention or treatment of esophageal cancer.

**Materials and Methods.** The information about the role and function of genes participating in the development of esophageal cancer were taken from GeneBank databases and publications. The mRNA nucleotide sequences of the human genes were derived from GeneBank (http://www.ncbi.nlm.nih.gov). The nucleotide sequences of miRNAs were taken from the article of London E. et al. [3]. Searching of miRNA’s target genes was performed by MiTarget program, created in our laboratory. This program defines the beginning of miRNA and mRNA binding sites: localization of binding sites in 5'-untranslated region (5'UTR), protein coding region (CDS), and 3'-untranslated region (3'UTR); free energy of interaction of miRNA with nucleotide sequence mRNA (ΔG, kJ/mole) and scheme of miRNA-mRNA nucleotides interaction.

**Results.** From the 68 candidate genes, participating in the development of esophageal cancer, only 54 genes were targets for miRNAs. The average free energy of binding of all miRNAs with mRNAs of all candidate genes in the 5’UTR region was equal -126 kJ/mole. The number of miRNA associations with mRNA having free energy of interaction greater than -125 kJ/mole is 16 from 87 associations of miRNA-mRNA in the 5’UTR. The miR-20-45152-5p, miR-2-3313-3p, miR-22-46979-5p and miR-1-155-3p form a cluster in mRNA of PTPRJ gene from 162 nt to 190 nt with a length 29 nt and average ΔG value equal to -132 kJ/mole. The whole length of all four binding sites was equal to 96 nt, that is three times more than the length of a cluster. The formation of a cluster of four binding sites in the 5’UTR of PTPRJ gene shows the ability of a given gene to compaction, which serves as the emergence of given miRNAs competition for the binding site. That is, from here it can be concluded that miR-2-3313-3p with a free energy of interaction equal -138 kJ/mole will occupy this binding site and will not allow other miRNAs to interact with this mRNA. Each miRNA has the binding site. That is, from here it can be concluded that miR-2-3313-3p with a free energy of interaction equal -138 kJ/mole will occupy this binding site and will not allow other miRNAs to interact with this mRNA. Each miRNA has the binding site.

Key words: LDL subclasses; LDL size; gradient gel electrophoresis; diabetes mellitus; children;

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