Abstract

Mitochondrial disorders, with incidence 1:5000 live births children, are one of the most common metabolic diseases. Clinically, it is heterogeneous group of disorders caused by mutations in more than 250 genes. Diagnostic of patients with suspected mitochondrial disorder relies on broad spectrum of biochemical analysis. One of them is a measurement of Mitochondrial Energy Generating Capacity (MEGC). The principle of MEGC analysis is measuring oxidations rate of ^{14}C – labeled substrates in 10 different incubations. These incubations contain [1-^{14}C]pyruvate, [U-^{14}C]malate or [1,4-^{14}C]succinate, donors and acceptors of Acetyl-CoA and inhibitors of TCA cycle. The results of MEGC analysis provide a variety of information about mitochondrial energy metabolism (MEM) of individual in particular tissue. In diagnostic of patients with suspected mitochondrial disorder is MEGC routinely determined in skeletal muscle. The aim of this study is to optimize MEGC analysis for its use in cultures skin fibroblasts. In sum, MEGC analysis was performed in 23 patients with primary deficiency of oxidative phosphorylation (OXPHOS), in 7 patients with secondary deficiency of OXPHOS and in 15 controls cell lines. The results of MEGC in cultured skin fibroblasts were then compared with results of spectrophotometric measurement of activity OXPHOS enzymes in fibroblasts and with selected patients the results of MEGC were compared with results of polarography in fibroblasts and with results of MEGC in skeletal muscle. In conclusion, MEGC analysis is more sensitive to detect disruption of MEM compared with spectrophotometry but only MEGC analysis is not sufficient for diagnostic of mitochondrial disorders. For more precise localization of OXPHOS deficiency, data obtained by several biochemical methods are necessary.