Contribution of GDF-15 and FGF-21 as potential diagnostic biomarkers for mitochondrial respiratory chain disorders.

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Abstract

Mitochondrial respiratory chain disorders (MRCD) are inherited neurological disorders that occur 1 in 5000 live births. Currently, muscle biopsy is the gold standard for diagnosis of MRCD due to the lack of sensitive biomarkers discovered. Growth differentiation factor-15 (GDF-15) and fibroblast growth factor-21 (FGF-21) have been proposed as potential biomarkers for detection of MRCD. This would be a very useful for first-line diagnostic tool, instead of the invasive muscle biopsy. We aimed to validate the utility of these two factors as promising biomarkers in MRCD using both biochemical and molecular tools. We evaluated 41 plasma samples from high-risk neurological symptom of MRCD (group1), 104 samples with non-high risk of MRCD but abnormal findings through screening tests (group2) and 45 samples from healthy control (group3) by ELISA. Skin fibroblasts from 9 high risk patients were tested for their GDF-15 and FGF-21 levels, super-complex 1-V immunological activity and mutation analysis. Statistically, the level of GDF-15 and FGF-21 in group1 were significantly high compared to the group3 (mean 84560 pg/ml±24808 SEM and 33086 pg/ml±25845 SEM respectively, p<0.05). In group2, GDF-15 and FGF-21 were elevated between 4-34 times compared to group3 (mean1017 pg/ml±167 SEM and 1467 pg/ml±515 SEM respectively, p<0.05). The area under receiver-operating-characteristic curve for GDF-15 was 0.7187±0.0556 SE indicating that it has a good discriminatory power in group1 compared to FGF-21 (0.6301±0.0603 SE). The overall sensitivity and specificity of GDF-15 for cut-off value of 300 pg/ml was 90.24% and 75.56% (p<0.05). However, we found no significant correlation between GDF-15 and FGF-21 (p value=0.465). GDF-15 shows more precise plasma/fibroblasts quantitative biomarker in comparison to FGF-21 in diagnosing of MRCD. This was supported by fibroblasts tests in which 5 out of 9 patients showed abnormal results in their protein immunological activity and mutations were detected.

Keywords: Biomarkers; respiratory chain disorders; GDF-15; FGF-21; fibroblasts

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