Plasma lipidomics reveals extensive lipid metabolism disruption in patients with glycogen storage disease type Ia

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BACKGROUND

Glycogen storage disease type Ia (GSDIa) is an inherited disorder of carbohydrate metabolism due to glucose-6-phosphatase deficiency. Although hyperlipidemia is a hallmark of GSDIa, its exact nature and consequences remain incompletely understood. Also, it can be resistant to current treatments¹. A lipidomic study was performed to further characterize hyperlipidemia in GSDIa².

PATIENTS

- 12 GSDIa patients (8 males, 4 females, age 5.2-34.9 years)
- 16 healthy controls (age- and gender-matched)
- 6 age-matched subjects with hyperlipidemia due to other conditions

METHODS

- 550 lipid species quantified on plasma by mass-spectrometry
  - Ceramides (Cer) (n=70)
  - Glycerophospholipids (LPC, PCaa, PCae) (n=90),
  - Bile acids (BA) (n=14),
  - Triacylglycerols (TG) (n=242)
  - Diacylglycerols (DG) (n=44)
  - Cholesterol esters (CE) (n=22)
  - Sphingolipids (SM) (n=15)
  - Fatty acids (FA) (n=12)

- Biochemical markers of metabolic control
RESULTS

GSDIa patients showed higher total Cer, PCaa, TG, DG and BA compared to both healthy controls and hyperlipidemic subjects and higher PCae, SM and CE compared to healthy controls.

AST value directly correlated with lysoPC a C26:1, lysoPCa and Cer(d18:0/20:0). LysoPC a C26:1 also directly correlated with cholesterol and ALT levels. Cer(d18:0/20:0) also directly correlated insulin levels.
DISCUSSION

Compared to previous studies focusing on traditional components (i.e. TG and cholesterol)\textsuperscript{3,4}, extensive lipidomics profiling of GSDI\textsubscript{a} patients showed broader lipid metabolism involvement possibly affecting various cellular functions (e.g., cell proliferation, insulin response) and highlighting currently unknown pathomechanisms in GSDI\textsubscript{a}. Specific lipid species may provide potential novel biomarkers for GSDI\textsubscript{a}.

REFERENCES