Introduction:

- The spectrum of lipid-induced changes in the secretion of hormones important in energy homeostasis has not yet been fully elucidated.
- Pattern of molecular responses to lipids depends largely on the route of administration based on studies done on incretins.
- Lack of placebo-controlled studies on the impact of exogenous lipids (IV and oral) on molecules important in energy homeostasis apart from incretins.
- What is the response to hyperlipidemia of molecules secreted by tissues affected by insulin resistance?
  - Liver: some evidence on the hepatokine fibroblast growth factor 21 (FGF-21) but limited knowledge on lipid induced changes in fetuin A levels.
  - Muscle and adipose tissue: lack of evidence on lipid induced physiological regulation of the myokine irisin and adipokine omentin.

The purpose of this study is to:

1. Differentiate the effects of oral vs. IV lipid administration on molecules related to insulin metabolism (insulin, c-peptide, glucagon, GLP-1 and GIP) and obesity (appetite regulators such as PYY, ghrelin, and leptin).
2. Investigate potential effects on novel molecules secreted by tissues affected by insulin resistance (i.e. muscle-irisin, liver-FGF-21 and fetuin A, and adipose tissue-olecine, adiponectin, and omentin).
3. Examine potential dose-dependent effect of lipids by comparing two concentrations of IV lipid emulsions

Materials & Methods:

- After a 10-hour overnight fast, twenty six subjects were randomized to one of four groups:
  - oral lipid group (n=6)
  - 20% intralipid IV lipid emulsion group (n=6)
  - 10% intralipid IV lipid emulsion group (n=5)
  - control group (saline infusion) (n=9)
- Blood samples were obtained at baseline and at 30-minute intervals for the first 2 hours and hourly thereafter.
- Main outcome measures: Circulating levels of insulin, glucose, c-peptide, FFA, incretins (GLP-1, GIP), glucagon, PYY, leptin, ghrelin, FGF-21, fetuin A, irisin, omentin and adiponectin were measured using commercially available ELISA or RIA assays. (Fig 1-4)

Statistical analysis

- SPSS version 17 (IBM, Armonk, NY) was used for data analysis. Data are presented as means ± standard deviation if normally distributed or as medians (with 1st and 3rd quartile) if non-normally distributed. (Table 1)
- Data were analyzed using ANOVA to depict the effect of the intervention excluding differences of baseline values between the groups. IAUCs were compared by univariate ANOVA and Bonferroni post hoc tests were used to compare groups. (Fig 1-4)

Conclusions:

- Metabolic responses to exogenous lipids depend on the route of administration.
- Prolonged administration of IV lipids triggers hyperinsulinemia without a concurrent decrease in glucose levels, a phenomenon observed in insulin resistant states.
- Importantly, only IV lipids trigger a dose dependent FGF-21 secretion which is non-glucagon-mediated.
- Orally administered lipids mostly affect gastrointestinal tract secreted molecules important in glucose and energy homeostasis such as PYY, incretins (GLP-1 and GIP), ghrelin as well as glucagon.
- Other novel molecules important in energy homeostasis such as irisin, omentin and fetuin A remained unaffected by lipids.

References:

- Thomassen K et al. Fasting plasma PYY levels and body fat content in insulin-resistant women. J Obes (Lond) 2014.

Table 1. Baseline characteristics of four groups (10% and 20% IV lipid-emulsion, intralipid and placebo groups)

Data expressed as mean ± standard deviation or normally distributed as median (1st and 3rd quartile). (Fig 1C) if the normally distributed