Efficacy of an extra virgin olive oil with a high content of polyphenols in the prevention of cardiovascular risk in patients with metabolic syndrome: preliminary results.

Aurelio Seidita,[1,2] Maurizio Soresi,[2] Lydia Giannitrapani,[2,3] Alessandra Cusimano,[2,3] Antonella Cusimano,[3] Giuseppa Augello,[3] Antonina Azzolina,[3] Juan Lucio Iovanna,[4] Roberta Chianetta,[2] Ida Muratori,[2] Antonino Terranova,[2] Melchiorre Cervello,[2] Anna Licata,[2] Antonio Carroccio,[1,2] Roberto Citarrella[2]

[1] Unit of Internal Medicine, "V. Cervello" Hospital, Ospedali Riuniti "Villa Sofia-Cervello", Palermo, Italy.
[2] Department of Health Promotion Sciences, Maternal and Infant Care, Internal Medicine and Medical Specialties (PROMISE), University of Palermo, Palermo, Italy.
[3] Institute for Biomedical Research and Innovation (IRIB), National Research Council, Palermo, Italy.
[4] Cancer Research Center of Marseille, Aix-Marseille University, CNRS, INSERM, Institut Paoli-Calmettes, CRCM, Marseille, France.

Background

Metabolic Syndrome (MS) is a global health problem resulting in a significant risk of cardiovascular events and mortality. Moreover, even if not included in the diagnostic criteria, liver steatosis is a common stigma of all the patients suffering from MS. It has been proved that the only effective, preventive MS treatment is lifestyle modification, with the increase of physical activity and the consumption of a balanced diet: the Mediterranean Diet (MD). Extra Virgin Olive Oil (EVOO), a food rich in monounsaturated fatty acids and polyphenols, has been reported to be the real added value of MD.

Objectives

The purpose of our study group was to evaluate the efficacy of the intake of a high-polyphenol content EVOO (HPPE) on anthropometric, clinical and laboratory parameters related to cardiovascular risk, metabolism, and liver function in two age, sex and BMI matched groups of MS patients.
Here, we present the preliminary results of the 1st-year of a 3-year study co-financed by the European Union - PON Research and Innovation 2014-2020 - DM1062/2021.

Methods

Thirty consecutive MS patients, all with liver steatosis, were enrolled and randomized, in a single-center double-blind prospective study, to add HPPE or standard EVOO (SE) (40 ml/daily for 6 months) to the MD.
Anthropometric/demographic measures, liver function, metabolic and inflammatory status, flow mediated dilatation (FMD), liver ultrasound and abdominal fat thickness (FT), were analyzed at baseline (T0) and after 6 months (T6). We further analyzed the gene expression pattern of some of the major pathways involved in systemic inflammation, oxidative stress, lipidic and glucose metabolism and development of hepatic steatosis, by extraction and subsequent amplification, via RT-PCR, of the RNA from peripheral blood mononuclear cells (PBMC).

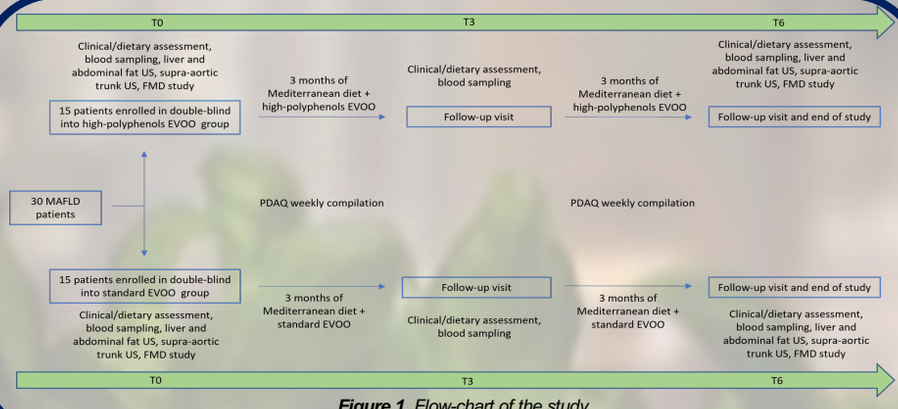

Figure 1. *Flow-chart of the study*

Results

Preliminary chemical analysis were performed on oils from 3 native cultivars (Biancolilla, Nocellara and Cerasuolo) coming from the same area of Western Sicily, milled with 4 methods (discs, hammers, opposing wheels and stoner). A Cerasuolo EVOO milled by opposing wheels was selected as HPPE. Patients had a very high compliance to dietary intervention, both considering MD and EVOO intake (mean PDAQ= 45). No differences were found at T0 between groups in all analyzed parameters. From T0 to T6, both groups showed a significant improvement in waist circumference (WC), glycated hemoglobinemia (HbA1C), and visceral FT ($p<0.05$). Only subjects in HPPE group had BMI, insulinemia, HOMA-IR, AST and subcutaneous FT improvement ($p<0.05$). No differences were observed at T6 between groups, even though a major reduction was shown in the HPPE group for BMI, WC, ALT, HbA1C, triglycerides, total and LDL-cholesterol, subcutaneous and visceral FT. A significant improvement of FMD ($p<0.002$) was reported in both groups, proving a reduction of endothelial disfunction. From T0 to T6 both groups showed reduction ($p<0.05$) of TRIB3 (known to be upregulated in insulin resistance mechanisms in adipose tissue) and SREBP expression (involved in the pathogenesis of steatosis and insulin resistance). We analyzed PNPLA3 (rs738409), TM6SF2 (rs58542926), PCSK9 (LOF) (rs1159114), PCSK9 (GOF) (rs505151) and GCKR (rs1260326) polymorphisms, proving that the minor allele frequency (MAF) in both HPPE and SE group are equivalent to those of the general population.

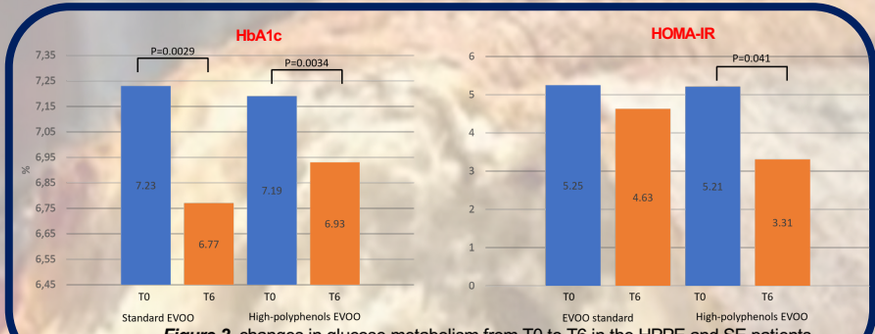

Figure 2. changes in glucose metabolism from T0 to T6 in the HPPE and SE patients

Conclusions

This preliminary analysis shows that the MD plus EVOO intake for 6 months can improve metabolic and cardiovascular parameters in MS subjects, improving anthropometric, clinical, insulin resistance and endothelial disfunction indexes. However, no differences at T6 were found between HPPE and SE groups, even though HPPE seems to potentially have more extended efficacy. No effect was proved regarding liver steatosis, even if we showed a consistent reduction of SREBP expression. This last evidence might suggest that MD plus EVOO intake might influence the metabolic and inflammatory pathways involved in liver steatosis development and that probably a longer duration (> 6 months) of this dietary intervention might reduce the degree of liver steatosis. Our preliminary data were most likely affected by the low number of patients, and we hope to prove significance while completing the study.

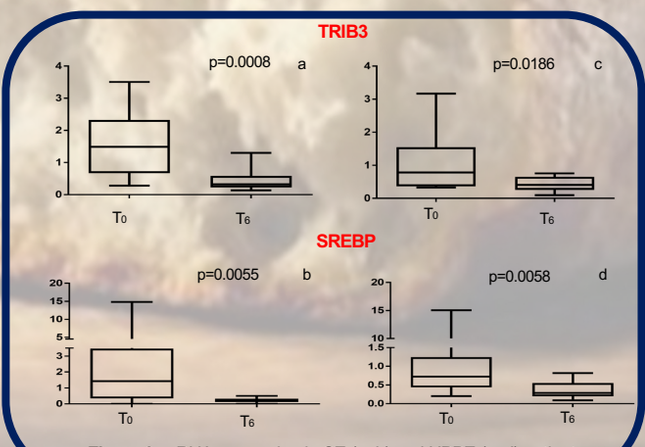

Figure 3. mRNA expression in SE (a, b) and HPPE (c, d) patients