Identification of medical complications and real-life care of familial and multifactorial chylomicronemia syndromes: the ESTHYM study

M Belhassen¹, E Van Ganse¹, M Ginoux¹ , M Nolin¹, H Bada², E Bruckert³, M Krempf⁴, V Rebours⁵, R Valero⁶, P Moulin²

¹ PELyon, PharmacoEpidemiology Lyon, Lyon, France, ² Hospices Civils de Lyon, INSERM UMR 1060 Carmen, Claude Bernard Lyon 1 university, France, ³ Pitié Salpêtrière University Hospital, APHP, Paris, France, ⁴Nantes University Hospital, Nantes, France, ⁵ BEAUJON University Hospital, APHP Clichy, France, ⁶ APHM University Hospital, Marseille, France

Introduction

Major hypertriglyceridemia is an established risk factor of acute pancreatitis and a controversial risk factor of ischemic cardiovascular disease.

The relative incidence of these events in hyperchylomicronemic patients exhibiting either recessive monogenic disorders i.e. familial chylomicronemia syndrome (FCS) or oligogenic predisposition with strong environmental interaction i.e. multifactorial chylomicronemia syndrome (MCS) is only inferred from retrospective studies.

The heterogeneity of hyperchylomicronemia syndromes prompted us to study prospectively the occurrence of major events in FCS and MCS.

Methods

- Genetic information, lipid phenotype and medical history collected before inclusion in electronic medical file from 4 tertiary lipid clinics
- Probabilist linkage with the “Système National des données de santé” (SNDS) the French National Health Insurance database, lists all reimbursed outpatient and inpatient medical resource use (claims data) for individuals covered by the general health insurance
- Observational study conducted on anonymized data,
- Approval by the French Institute for Health Data (Institut National des Données de Santé, approval n° TPS 23941, on December 19, 2017)
- Approval by The National Informatics and Liberty Committee (approval n°917259 on March 1, 2018).
- Written information sent to each patient in agreement with the French law of bioethics

- Control subjects fully matched 1/3 for age, sexe, area of residency and income

Results

	FCS		MCS		Control FCS		Control MCS		FCS vs. MCS	FCS vs. control	MCS vs. control
	(n=30)		(n=124)		(n=83)		(n=326)		(p-value)	(p-value)	(p-value)
	n	%	n	%	n	%	n	%			
Gender											
Males	12	40.0%	84	67.7%	35	42.2%	220	67.5%	0.0049	ns	ns
Females	18	60.0%	40	32.3%	48	57.8%	106	32.5%			
Age (years)											
Mean - SD	34.1	13.3	45.0	12.4	35.0	13.7	45.4	12.6	<0.0001	ns	ns
BMI											
<25	19	69.9%	37	30.6%	-	-	-	-	<0.0001	na	na
25 - 30	8	26.7%	45	36.3%	-	-	-	-			
>30 - 35	1	3.3%	24	23.1%	-	-	-	-			
Diabetes before MCS/FCS diagnosis	0	0%	16	12.9%	1	1.2%	8	2.5%	0.0426	ns	0.0002
Treatment during FU											
Fibrates	22	73.3%	91	73.4%	2	2.4%	9	2.8%	0.99	<0.0001	<0.0001
HMG CoA reductase inhibitors	10	33.3%	59	47.6%	12	14.5%	45	13.8%	0.15	0.0180	<0.0001
Omega-3-FA	12	40.0%	32	25.8%	0	0%	2	0.6%	0.12	<0.001	<0.0001

OUTCOMES	FCS (n=30)		MCS (n=124)		Control FCS (n=83)		Control MCS (n=326)		FCS vs. MCS (p-value)
	n	%	n	%	n	%	n	%	
Acute Pancreatitis									
Number of patients with AP during FU	15	50.0%	25	20.2%	0	0%	1	0.3%	<0.0001
Number of stays	9.3	10.2	2.1	1.7	-	-	-	-	0.1374
Mean – SD									
Duration of stay (number of night)	6.5	6.4	8.8	8.8	-	-	-	-	ns
Mean – SD									
Hospitalizations for CVD during FU	2	6.7%	31	25.0%	2	2.4%	8	2.5%	0.0296
Cardiovascular diseases									
Acute myocardial infarction	1	3.3%	4	3.4%	1	1.2%	1	0.3%	ns
Cerebral infarction	0	0 %	1	0.8%	0	0%	1	0.3%	
Transient cerebral ischemic attacks and related syndromes	0	0 %	2	1.6%					
Diabetes occurrence following FCS/MCS diagnosis	7	23.3%	36	29.0%	2	2.4%	5	1.5%	0.5324

Hosp for CVD
FCS vs CTRL FCS HR=3.0 [0.7 ; 11.9] p=0.13
MCS vs CTRL MCS HR=10.3 [4.8 ; 22.2] p<0.01

Conclusions

- The incidence of acute pancreatitis is very high in FCS and MCS with previous history of acute pancreatitis
- the incidence of hospitalization for cardiovascular disease is increased in MCS only.
- These data illustrate the severity of these rare diseases.
- Differences in TG rich lipoproteins metabolism and comorbidities in MCS vs FCS drives the occurrence of different pattern of complications.