CIRCULATING LIVER SPECIFIC miR-122 IN END STAGE RENAL DISEASE ON MAINTENANCE HEMODIALYSIS

Rivoli Laura , Vliegenthart AD Bastiaan , Van Bragt Job , Tzoumas Nikos , Dear W. James , Neeraj Dhaun

University/BHF Centre for Cardiovascular Science, The Queen's Medical Research Institute, University of Edinburgh, United Kingdom

Introduction and objectives

Liver specific microRNA-122 (miR-122) is a sensitive and specific circulating biomarker that is being qualified for use in the clinical management of a range of liver diseases and for hepatotoxicity screening in drug development. It has been reported that kidney dysfunction is associated with a significant reduction in the concentration of circulating microRNAs. Haemodialysis is a common treatment for acute kidney injury and end-stage renal disease (ESRD). The impact of haemodialysis on circulating microRNAs is variable with some microRNAs significantly reduced by haemodialysis. The objective of this study was to determine the effect of ESRD and haemodialysis on miR-122

Methods

Blood samples were collected from 17 patients with ESRD on maintenance haemodialysis and 17 matched healthy controls. All subjects had standard liver function tests in their respective normal ranges. Samples from ESRD patients were collected pre- and post-haemodialysis. MiR-122 and spiked-in cel-miR-39 were measured by qPCR.

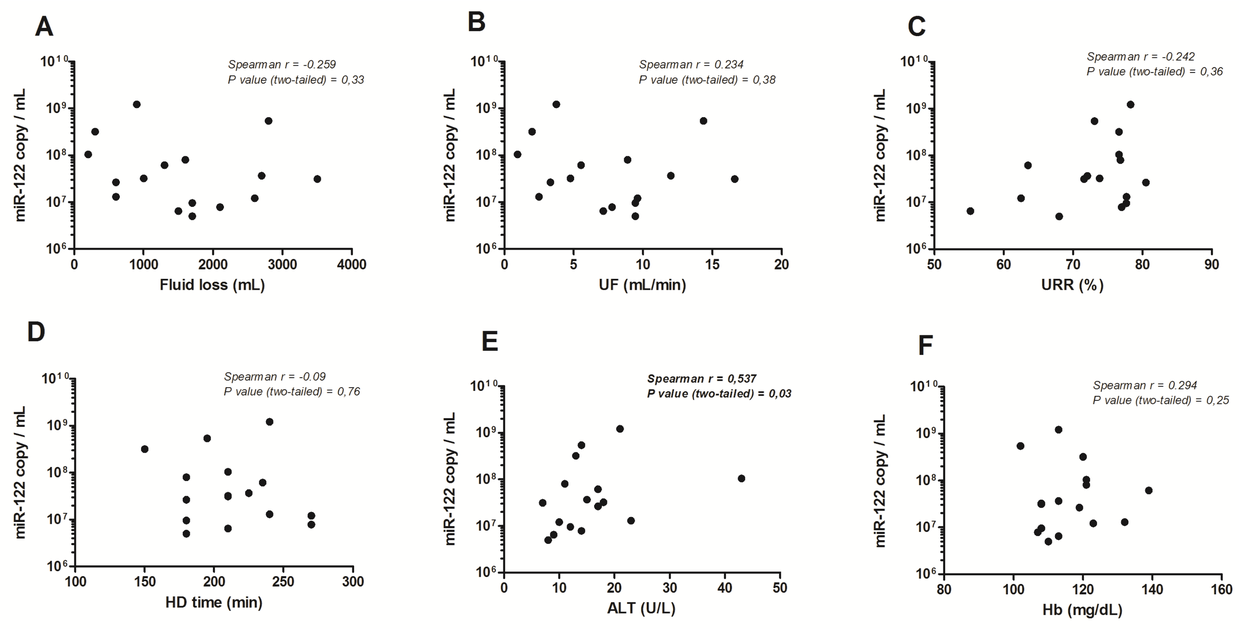
Population
- 17 patients on standard maintenance hospital based HD and 17 matched healthy controls
- Filter system: polysulfone high-flux dialyzer (Fx 800), 1.8 m2 effective surface area, inner lumen 210 mm, wall thickness 35 mm, Fresenius Medical Care, Molecular weight cut off (MWCO): 30 kDa

Collection
- Pre- and post-HD blood samples
- Post filter spent dialysate was collected at end of the routinely dialysis session

RNAisolation
- RNA wasisolated from 50µl plasma, serum and dialysate samples using the miRNeasy Serum/Plasma Kit (Qiagen, Venlo, Netherlands)

MiRNA analysis
- RNA was reverse-transcribed with the miScript reverse transcription kit (Qiagen).
- Quantitative PCR was performed using the miScript SYBR-green PCR kit (Qiagen).
- CDNA synthesis and real-time PCR was performed using the miScript PCR System.

Figure 3: Correlation (r) and significance (P) of associations between Micro RNA 122 abundance in plasma and laboratory measurements in 17 ESRD on HD



Conclusions

MiR-122 is lower in ESRD compared to health. Haemodialysis restores circulating miR-122 concentration to healthy levels. This should be considered when interpreting liver injury using miR-122 in patients with ESRD and specific reference ranges that define normal in this setting may need to be developed.

References

Turchinovich A. Et al. Characterization of extracellular circulating microRNA. Nucleic Acids Res. 2011

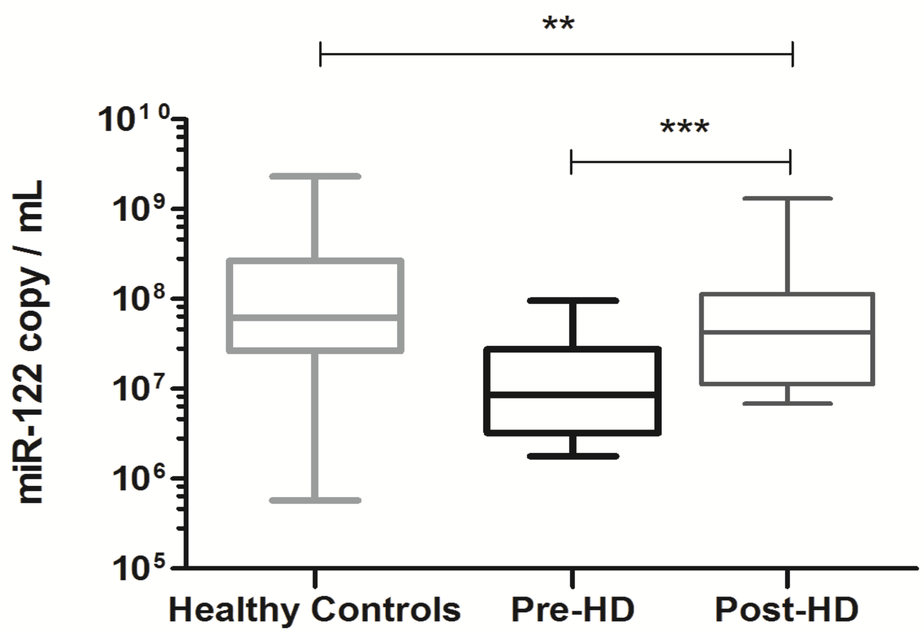
Emilian C. Et al. MicroRNAs in patients on chronic haemodialysis (MINOS study). Clin J Am Soc Nephrol. 2012

Results

There was no difference in miR-39 concentration across healthy controls and ESRD patients, pre- and post-haemodialysis. Pre-HD miR-122 circulating concentration was 13-fold lower compared with healthy controls (pre-HD mean: 21.7 million copies/mL [95% CI 6.7 – 37 million]; healthy controls mean: 284 million [95% CI 8.9 – 650 million] copies/mL) (p=0.044 two-tailed). With HD there was a 8-fold increase in miR-122 to 168 million (95% CI 2.6 – 340.1 million) copies/mL (Wilcoxon matched-pairs signed rank test p<0.0005 two-tailed). There was no significant difference between miR-122 post-HD and concentrations in health (p=0.47 two-tailed Mann-Whitney test). The increase in miR-122 did not correlate with changes in urea, blood pressure, haematocrit or degree of ultrafiltration and fluid removal

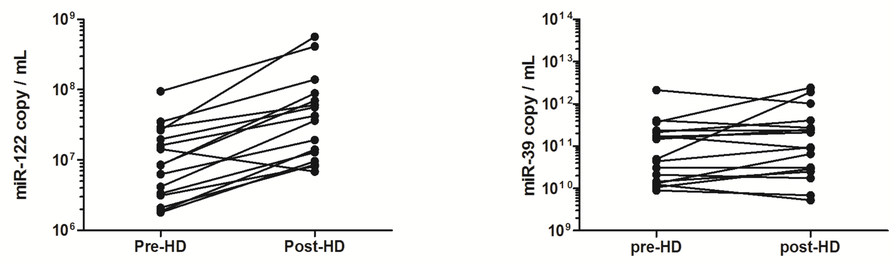
	Haemodialysis	Healthy Controls	*p*
Number of patients	17	17	
Age (years)	58±13	54±8	ns
Sex			
M % (n)	47 (8)	53 (9)	ns
T2DM % (n)	29 (5)		
Hypertension % (n)	70 (12)		
BMI (kg/m²)	26.9±6	26.3±4	ns
SBP (mmHg)	130±20	130±13	ns
ALT (U/L)	15±8	22±9	ns
Bil (µmol/L)	9.2±3	9.2±4	ns
CRP (mg/dL)	10±15	2±1	0.058
Haemoglobin (mg/dL)	114±12	145±11	<0.001

Figure 1: Plasma concentration of MicroRNA 122



***Wilcoxon matched-pairs signed rank test Pre-HD vs. Post-HD *p*<0.0005 (Two-tailed); ** Mann Whitney test Pre-HD vs. Healthy Controls *p*=0.004 (Two-tailed); Post-HD vs. Healthy Controls *p*=0.47

Figure 2: (A) Plasma concentration of MicroRNA 122 pre and post a single dialysis session. (B) Plasma concentration of MicroRNA 39 before and after dialysis



*To whom correspondence should be addressed: rivolilaura@yahoo.it

printed by MegaPrint Inc. www.postersession.com

243-SP
53 ERA
Chronic Kidney Disease. Lab methods, GFR measurement, urine proteomics.
Laura Rivoli
DOI: 10.3252/pso.eu.53era.2016
ePosters supported by F. Hoffmann- La Roche Ltd.
53rd CONGRESS ERA-EDTA VIENNA AUSTRIA MAY 21st-24th, 2016
PosterSessionOnline.com