Circulating Exosomal Mir21 And Mir320 In Obstructive Sleep Apnea

D. Sanz-Rubio[1], I. Martin-Burriel[2], V. Gil[1], J. M. Marin[1]

[1]Hospital Universitario Miguel Servet, Zaragoza, Spain, [2]LANGEBIO, Faculty of Veterinary, Zaragoza, Spain

Corresponding author's email: jmmarint@unizar.es

Rational. Epidemiological studies indicate that there may be an association between obstructive sleep apnea (OSA) and cardiovascular and metabolic diseases. Some pro-inflammatory miRs (miR-21, miR320) critical for the immune response or hypoxia are often overexpressed in cancers and atherosclerosis.

Aim. To examine the expression of miR-21& miR320 in circulating exosomes from patients with OSA.

Methods: From a Sleep Unit and in the frame of a long-term longitudinal cohort study we selected 65 non-smokers OSA patients (apnea-hypopnea index –AHI- 30 events/h) and 26 age, gender and BMI-matched controls (AHI < 5). All participants were free of comorbidities other than OSA at baseline (GovTrials, NCT014575421). At recruitment and yearly, carotid ultrasound was performed and subclinical atherosclerosis (SA) was defined as by the presence of carotid plaques of by an intima-media thickness > 0.85 mm. Plasma-derived exosomes were isolated by precipitation using miRCURY™ Exosome Isolation Kit. Exosomes were characterized by transmission electron microscopy, dynamic light scattering assay and Western Blot analysis using CD63 and HSP70. Exosome total RNA was obtained using miRCURY™ RNA isolation kit. miR-21-5p and miR-320-3p were analysed by real time quantitative PCR (RT-qPCR) using miRCURY LNA™ technology.

Results:

At baseline, expression of both plasma exosomes miR-21-5p and miR-320a-3p were increased in patients with OSA compared to controls (Fold Change (FC): 2.69 and 1,81 respectively ($p<0.01$)). FC expression was higher in the OSA patients with SA than in patients without SA: 2,47±2,19 vs 1,65±0,69 for miR21-5p ($p<0.02$) and 1,98±1,10 vs 1,46±0,72 ($p<0.05$) respectively. At one-year follow-up, expression of 320a-3p did not change in patients treated with CPAP (n=40) or non-treated (n=25) whatever the SA status was at baseline. However, miR-21-5p showed a persistent overexpression among non-treated OSA patients with SA (3,77±3,71) and a decreased in patients treated with CPAP (1,49±1,19, $p <0.01$).

Conclusions. Circulating exosomes cargo of miR-21-5p and miR-320a-3p are increase in patients with OSA and subclinical atherosclerosis. After one year of effective treatment with CPAP in OSA patients, circulating exosomal miR-21-5p decrease in those with subclinical atherosclerosis. This study suggest that this miRNA may play a role as an intermediary mechanism in cardiovascular morbidity in OSA.

Supported by Instituto Carlos III, Ministry of Health (PI/2175 & PI/1940)

This abstract is funded by: Instituto Carlos III, Ministry of Health (PI/2175 & PI/1940)