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P-002: THE ROLE OF FETUIN-A IN VASCULAR AGING IN THE RAT AORTA

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Introduction

Fetuin-A is a prevalent anti-inflammatory glycoprotein that resists proinflammatory cytokine production. Low fetuin-A levels indicate an increased risk for cardiovascular diseases. As fetuin-A levels decrease, the production of inflammatory cytokines increases as a result of adipocyte-related inflammation. With this study, the natural aged rat model that we created for two years, we aimed to predict fetuin-A in the natural senescence process with vascular especially aortic aging and possible affected inflammation markers.

Methods

Sixteen Wistar albino male rats were equally divided into two groups as the young (<12 months) group and the elderly (>24 months) group. The thoracic aorta was excised for analysis. The effect of aging on the aorta, proliferation, oxidative stress and inflammation markers were evaluated by Real Time Polymerase Chain Reaction method. Histological evaluation was performed to confirm the findings related to aging, and serum sampling was performed to determine fetuin-A levels.

Table-1: The results of the gene expression analysis with biochemical analysis of fetuin-A

	young rats	elderly rats	p values
Fetuin-A, mean ± SD	14.99 ± 2.86	11.06 ± 2.11	0.007
SOD-1 (median)	1.06	0.44	0.25
TNF-α (median)	1.01	1.13	0.4
IL-1β (median)	1.001	1.68	0.06
IL-6 (median)	1.007	0.099	0.000
NF-κB (median)	0.97	1.074	0.88
TGF-β (median)	0.97	2.74	0.28
i-NOS (median)	1	812.3	0.006
e-NOS (median)	0.98	3.65	0.001
Ki-67 (median)	0.97	1.59	0.75
PDGFR-β (mean ± SD)	1.02 ± 0.22	0.83 ± 0.67	0.46

Abbreviations: **SOD-1**: Superoxide dismutase-1; **TNF-α**: Tumor necrosis factor-α; **IL-1β**: Interleukin-1β; **IL-6**: Interleukin-6; **NF-κB**: Nuclear factor-κB; **TGF-β**: Transforming growth factor-β; **i-NOS**: Inducible nitric oxide synthase; **e-NOS**: Endothelial nitric oxide synthase; **Ki-67**: a protein known as a proliferation marker; **PDGFR-β**: Platelet-derived growth factor receptor-β.

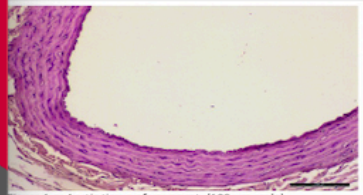


Figure 1-a: Aortic tissue of young rat. (100 µm scale)

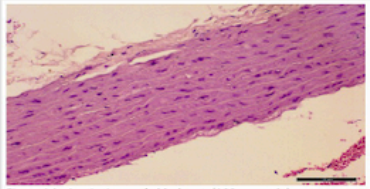


Figure 1-b: Aortic tissue of elderly rat. (100 µm scale)

Results

When compared to the young tissue, the expression of TGF-β, TNF-α and IL-1β was increased in the elderly group but the results were not statistically significant. The anti-oxidative capacity was slightly decreased in aged tissue.

In the histological study, inflammatory responses were confirmed in the elderly group with degenerated cardiomyocytes with irregular myofibrils, in contrast to the findings in the young tissues. (Figure 1a,1b). While the mean Fetuin-A level was 14.99 ± 2.86 in young rats, it was 11.06 ± 2.11 in elderly rats and the difference between the groups was statistically significant (p=0.007) (Table-1).

IL-6 levels which are inflammatory markers were also lower in elderly group (1.007 versus 0.099; p<0.001) and there was a correlation between Fetuin-A and IL-6 levels (r: 0.56; p=0.03). While there was no significant difference of antioxidant capacity assessed by SOD, the oxidative stress markers were significantly higher in elderly rats than young's (i-NOS: 1.0 vs. 812.3, p=0.006; e-NOS: 0.98 vs. 3.65, p=0.001). There was a correlation between Fetuin-A and e-NOS (r: -0.56; p=0.024) (Table-1).

Conclusion

Vascular senescence causes cell damage through inflammatory responses. Fetuin-A, which is easily measured in blood, significantly reflects the changes seen secondary to vascular aging.

Therefore, fetuin-A may be a marker of pathologies that should be evaluated and clarified in early vascular injury.

These preliminary studies may further elucidate the principles of vascular aging prevention and cardiovascular protection.