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Evaluation of advanced glycation end product and antibodies against oxidized low-density lipoproteins levels in patients with neuroendocrine tumors based on tumor location

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pharmaceuticals MDPI

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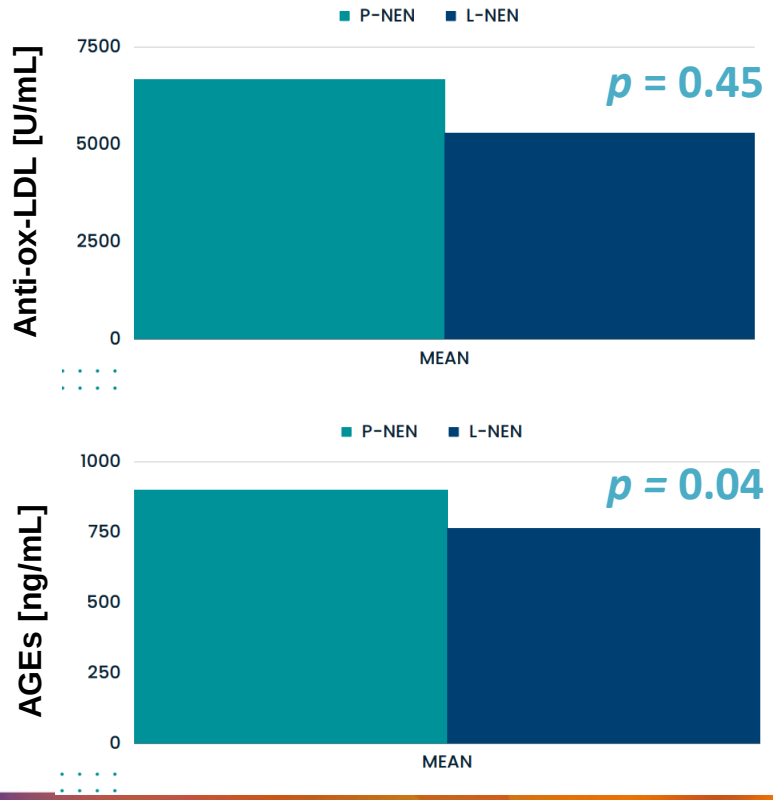
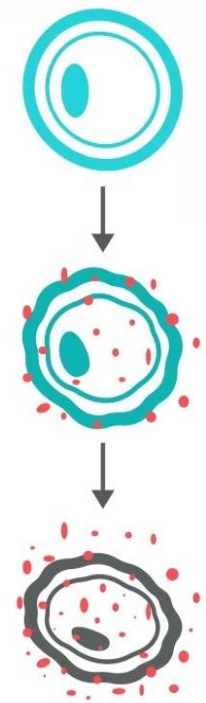
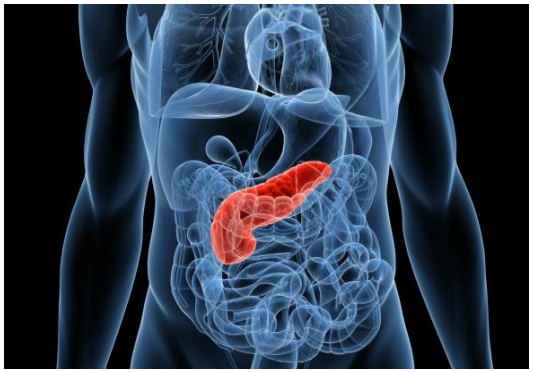
Graphical Abstract

OXIDATIVE STRESS





NEUROENDOCRINE TUMORS



Abstract:

Neuroendocrine neoplasms (NENs) are recognized as a heterogeneous group of tumors derived from neuroendocrine cells present in multiple organ systems. The importance of early and precise detection of NENs for effective treatment outcomes is well-understood. Biochemical markers such as antibodies against oxidatively modified low-density lipoproteins (anti-oxLDLs) and advanced glycation end products (AGEs) could be correlated with the presence and type of these tumors. In this study, an attempt was made to assess the levels of anti-oxLDLs and AGEs in patients diagnosed with NENs, with a tumors located in the lung and pancreas. A total of 20 patients were studied, equally divided between pancreatic NENs (P-NENs) and lung NENs (L-NENs). Venous blood samples from these patients were collected and processed to obtain serum. The levels of anti-ox-LDLs and AGEs were then quantified using the enzyme-linked immunosorbent assay (ELISA) technique. Results were presented as mean values with the standard error of the mean (SEM), and a *p*-value of less than 0.05 was considered to denote statistical significance. In the findings, anti-oxLDL levels in the P-NEN group were found to average at 6649.000 ± 1445.922 U/mL, while those in the L-NEN group were 5283.000 ± 1016.513 U/mL. A significant difference between these groups was not observed. On the other hand, a significant variation in AGE concentrations was noted: 898.509 ± 27.382 ng/mL for P-NEN patients compared to 763.106 ± 55.143 ng/mL for L-NEN patients. In conclusion, this preliminary findings suggest that AGE concentrations could be a potential biomarker for distinguishing between pancreatic and lung NENs.

Keywords: advanced glycation end products; biomarker; neuroendocrine neoplasms; oxidatively modified low-density lipoproteins

Introduction

Neuroendocrine neoplasms (NENs), are tumors originating from neuroendocrine cells located in different organ systems.

In order to increase the detection of NENs, attempts should be made to correlate various biochemical markers with the presence of NENs, such as antibodies directed against oxidatively modified low-density lipoproteins (anti-ox-LDLs) and advanced glycation end products (AGEs).

Determination of plasma anti-ox-LDLs levels allows assessment of the intensity of lipid peroxidation processes in the patient's body.

AGEs, accumulating in tissues, significantly increase the level of oxidative stress in the body, which has been linked to the development of NENs.

Introduction - materials and methods

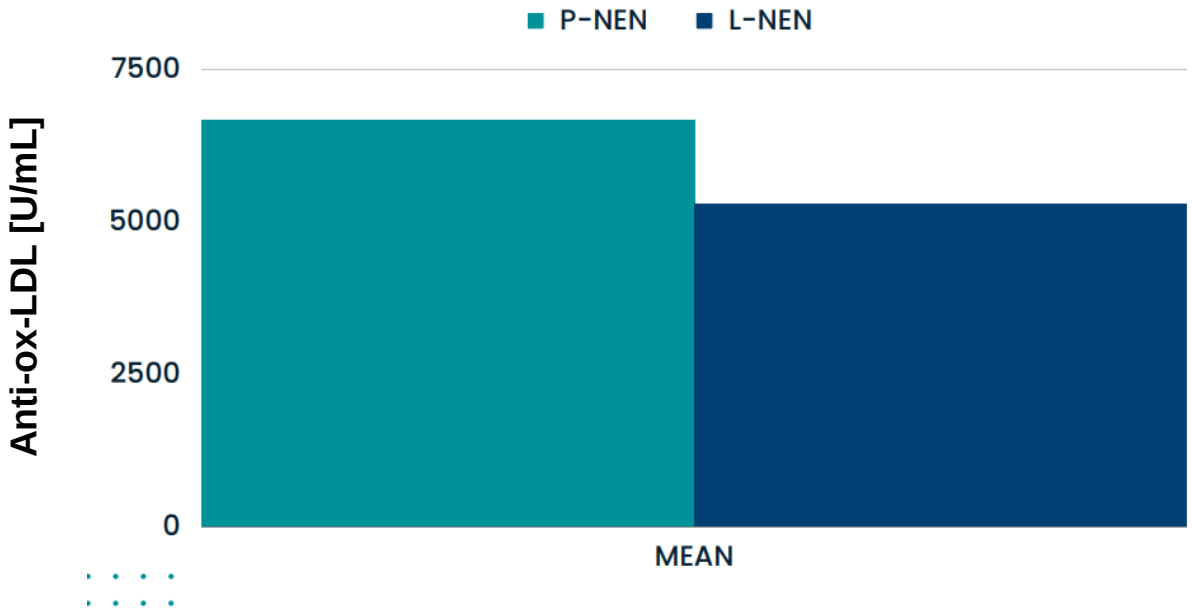
1. Patients were equally divided into two groups: Pancreatic NENs (P-NENs) and Lung NENs (L-NENs), with 10 patients in each group.
2. The study material consisted of blood serum samples from patients diagnosed with neuroendocrine tumors.
3. The levels of antibodies against oxidatively modified low-density lipoproteins (anti-oxLDLs) and advanced glycation end products (AGEs) in blood serum were quantified. The quantification was performed using the enzyme-linked immunosorbent assay (ELISA) technique.

Introduction - characteristics of the study participants

Anthropometric characteristic of the patients with pancreas and lung cancer divided according to the localization of the tumor. Each value is mean ± SEM. A *p*-value of less than 0.05 was considered statistically significant.

	P-NEN	L-NEN	*p*-value
n	10	10	-
Sex (f/m)	6/4	5/5	0.6733
Age [yrs]	63.50 ± 3.76	56.50 ± 2.86	0.9666
Body mass [kg]	84.50 ± 1.22	80.50 ± 3.67	0.3511
Height [cm]	171.40 ± 2.01	173.00 ± 2.71	0.5034
BMI [kg/m^2]	28.05 ± 0.73	26.35 ± 1.45	0.7658

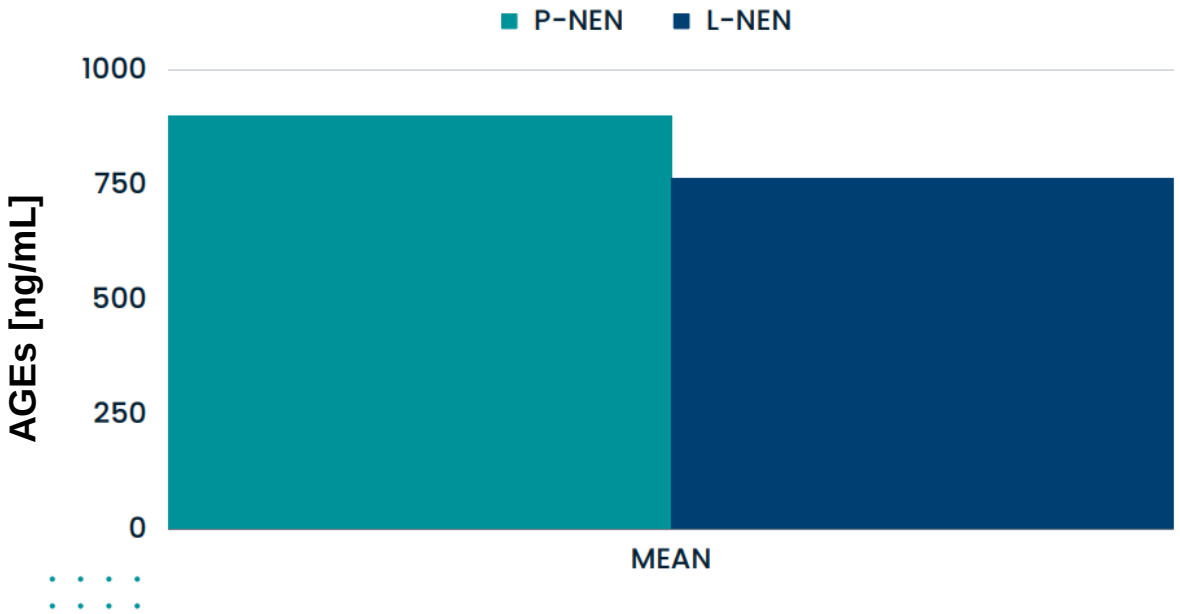
Results and discussion - Anti-ox-LDL



$p = 0.45$

Anti-ox-LDL [U/mL]	P-NEN	L-NEN	*p*-value
Mean	6649	5283	0.45
SEM	1446	1017	

Results and discussion - AGEs



$p = 0.04$

AGEs [ng/mL]	P-NEN	L-NEN	*p*-value
Mean	898.5	763.1	0.04
SEM	27.4	55.1	

Conclusions

- The data reflected a lack of significant difference in the anti-oxLDL levels between the two patient groups, thus indicating that anti-oxLDLs may not serve as a reliable distinguishing biomarker for P-NENs and L-NENs.
- Contrarily, a notable disparity in AGE concentrations between the two groups was observed, with higher levels identified in P-NEN patients, suggesting the potential of AGEs as a promising biomarker for distinguishing between pancreatic and lung NENs.
- These preliminary findings contribute to the ongoing efforts toward improving the diagnostic accuracy and subsequent management of NENs, although further research is warranted to validate the utility of AGEs as a biomarker.

Acknowledgments

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References

- Hajam, Y.A.; Rani, R.; Ganie, S.Y.; Sheikh, T.A.; Javaid, D.; Qadri, S.S.; Pramodh, S.; Alsulimani, A.; Alkhanani, M.F.; Harakeh, S.; et al. Oxidative Stress in Human Pathology and Aging: Molecular Mechanisms and Perspectives. Cells 2022, 11, 552, doi:10.3390/cells11030552.
- Kawasaki, K.; Rekhtman, N.; Quintanal-Villalonga, Á.; Rudin, C.M. Neuroendocrine Neoplasms of the Lung and Gastrointestinal System: Convergent Biology and a Path to Better Therapies. Nat. Rev. Clin. Oncol. 2023, 20, 16–32, doi:10.1038/s41571-022-00696-0.
- Perrone, A.; Giovino, A.; Benny, J.; Martinelli, F. Advanced Glycation End Products (AGEs): Biochemistry, Signaling, Analytical Methods, and Epigenetic Effects. Oxid. Med. Cell. Longev. 2020, 2020, 1–18, doi:10.1155/2020/3818196.
- Shen, C.-Y.; Lu, C.-H.; Wu, C.-H.; Li, K.-J.; Kuo, Y.-M.; Hsieh, S.-C.; Yu, C.-L. The Development of Maillard Reaction, and Advanced Glycation End Product (AGE)-Receptor for AGE (RAGE) Signaling Inhibitors as Novel Therapeutic Strategies for Patients with AGE-Related Diseases. Molecules 2020, 25, 5591, doi:10.3390/molecules25235591.
- Zhou, Y.; Zhang, A.; Fang, C.; Yuan, L.; Shao, A.; Xu, Y.; Zhou, D. Oxidative Stress in Pituitary Neuroendocrine Tumors: Affecting the Tumor Microenvironment and Becoming a New Target for Pituitary Neuroendocrine Tumor Therapy. CNS Neurosci. Ther. 2023, 29, 2744–2759, doi:10.1111/cns.14315.