

Review Article**Copeptin and Hypertension : a Scoping Review of Literature**

Farnoosh Ebrahimzadeh¹, Dadkhoda Soofi*², Farhad Soufi³

1. Department of Internal Medicine, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
2. Internal of Medicine, Faculty Member, Department of Medicine, Zabol University of Medical Sciences, Zabol, Iran.
3. Islamic Azad University, Tehran Medical Branch Tehran, Iran.

***Corresponding Author:** Dadkhoda Soofi, Internal of Medicine, Faculty Member, Department of Medicine, Zabol University of Medical Sciences, Zabol, Iran. ORCID: <https://orcid.org/0000-0002-8867-3044>

Abstract:

Introduction: Copeptin is a stable molecule and it is easily measured by using a rapid method. Serum concentration of coupeptin will be increase in several clinical conditions like as hypertension.

Methods: This review study was conducted by using keywords such as Copeptin, Blood Pressure, Disease Search, reputable scientific databases in Google Scholar, laparoscopy, Surgical technician, surgery and by searching reputable scientific databases in Google Scholar, PubMed, Science Direct, Web of Science, Ovid Medline, WHO site , and dissertations received during the years 2000 to 2021, and finally 20 sources were selected and criticized, interpreted and analyzed.

Results and conclusion: It seems that new biomarkers such as copeptin to be needed to make faster treatment decisions and better prognostic assessments for heart disease and hypertension..

Keywords: Surgical Technician, Laparoscopic, Surgery

Submitted: 29 March 2022, Revised: 12 May 2022, Accepted: 4 June 2022

Introduction

Cardiovascular disease is one of the most important and common causes of death and disability, especially in developing countries. According to statistics, more than one billion and one hundred and thirty million people in the world suffer from high blood pressure. This disease is a risk factor for stroke, chronic renal failure and peripheral vascular disease (1,2). The most important feature of hypertension is asymptomatic that it is also called the silent killer. On the other hand, advanced equipment is not required for its diagnosis and its control is easily possible with changes in lifestyle and drug treatment (3, 4). Any factor that upsets the hemostatic balance of the body is considered a stress factor. Any stress that stimulates the hypothalamus, pituitary and adrenal axis causes an increase in AVP (arginine vasopressin). Copeptin was first described in 1972 by Holwerda, 39 amino acid glycopeptide rich of nucleus with a leucine. Copeptin is the c-terminal portion of proopiomelanocortin which vasopressin is also composed of it (5, 6). Determining its concentration as a more stable protein indirectly proves the amount of synthesized anti-diuretic hormone. Copeptin is a glycosylated peptide derived from the leading gap in arginine-vasopressin production. Unlike arginine and vasopressin, copeptin is a stable molecule and it is easily measured by using a rapid method. Serum copeptin concentration will be increase in several clinical conditions, including hypertension and chronic kidney disease of particular interest is the study of cardiovascular disease. The need for faster diagnosis, better assessment of prognosis and treatment decisions in various diseases is related to the research and study of new biomarkers (7). Diagnosis and prognosis for some diseases can be very time consuming and tedious. This is why new biomarkers such as Copeptin are needed to make faster treatment decisions and better prognostic assessments for heart disease and hypertension. The purpose of this study was

to investigate the relationship between copeptin and blood pressure in this review study.†

Materials and Methods

This review study was conducted by a narrative review method and keywords such as Copeptin, Blood Pressure, Disease search in international scientific databases including: Pub Med, Web of Science, Google Scholar, Scopus, Elsevier, and internal scientific databases including: Barakatns knowledge system (barakatns), scientific jihad database, Iranian medical library (medlib), national journals database (magiran), knowledge reference (civilica) and search on WHO site were performed. A total of 58 scientific sources were collected, including books, articles, dissertations and reports that were published in Persian and English between 2000 and 2021 on Copeptin, blood pressure, and disease. Unrelated sources and articles were removed and sources related to our review were studied. Finally, 33 articles and scientific sources were selected and analyzed according to the purpose of the study and according to the needs of 20 articles.†

Results

In recent years, there have been many articles on the role of plasma copeptin in metabolic syndrome [8], obesity [9] and the progression of chronic kidney disease [10, 11]. Copeptin is a 9-amino acid peptide that has a cyclic structure and is derived from the precursor of AVP precursor. AVP pro-Pre is a pro-hormone synthesized by the supraoptic nuclei of the hypothalamus and transmitted to the posterior pituitary (neurohypophysis) through hypothalamic axons inside vesicles. This prohormone is degraded during axonal transport to the neurohypophysis by an enzyme cascade consisting of 4 enzymes: signal peptide-4, Copeptin-3, neurofizin-2, AVP-1. Water is from the kidneys which is produced in homolar ratio in the hypothalamus and processed during axonal transport. Copeptin has been identified

as an independent predictor of heart failure and adverse heart events, and elevated copeptin levels have been associated with increased mortality in patients with hypertrophic cardiomyopathy. Its main function remains unknown in the blood. The rate of 1.7-11.25 pmol / L is normal. It is more common in men than women and its concentration does not depend on age and glomerular filtration except in people with AMI. Because copeptin is secreted into the bloodstream in equal amounts to AVP; Its amount reflects the amount of AVP output. Since it has a longer half-life than AVP, it can be used as an alternative to measuring AVP. Copeptin is released in equal amounts with circulating AVP; Measuring it can provide valuable information about the severity of ADPKD. Higher concentrations of copeptin are associated with impaired renal function, decreased renal blood flow, larger kidneys, and albuminuria. Copeptin is associated with plasma osmolarity but is less secreted by volume, osmolarity, and urea, and these relationships are the same in males and females and are independent of age and using the diuretics. Water is from the kidneys which is produced in homolar ratio in the hypothalamus and processed during axonal transport. Copeptin has been identified as an independent predictor of heart failure and adverse heart events, and elevated copeptin levels have been associated with increased mortality in patients with hypertrophic cardiomyopathy. Its main function remains unknown in the blood. The rate of 1.7-11.25 pmol / L is normal. It is more common in men than women and its concentration does not depend on age and glomerular filtration except in people with AMI. Because copeptin is secreted into the bloodstream in equal amounts to AVP; Its amount reflects the amount of AVP output. Since it has a longer half-life than AVP, it can be used as an alternative to measuring AVP. Copeptin is released in equal amounts with circulating AVP; Measuring it can provide valuable information about the severity of ADPKD. Higher concentrations of copeptin

are associated with impaired renal function, decreased renal blood flow, larger kidneys, and albuminuria. Copeptin is associated with plasma osmolarity but is less secreted by volume, osmolarity, and urea, and these relationships are the same in males and females and are independent of age and using the diuretics. ¹

Discussion and Conclusion

Many studies have shown that increasing the concentration of copeptin is associated with renal failure and copeptin is negatively associated with estimating glomerular filtration rate (eGFR) (13, 14). In most studies, copeptin was positively associated with albumin / urinary protein excretion [5]. Population-based studies have shown that copeptin is strongly associated with microalbuminuria (15). Recent evidence suggests that high blood pressure is associated with increased the copeptin levels. For example, in adolescents with hypertension, copeptin levels were higher in adolescents with normal hypertension. Not only office hypertension but also outpatient hypertension (both systolic and diastolic) was associated with copeptin levels [16-17]. In another recent study, the relationship between copeptin and refractory hypertension was investigated. Initial plasma copeptin concentrations were positively correlated with male sex, plasma osmolality, BP and negatively correlated with glomerular filtration rate (18). Studies have also shown that copeptin concentrations are significantly higher in patients with suspected acute ACI (acute coronary syndrome) than in patients with suspected ACS but other definitive diagnoses. These other final diagnoses can be unstable angina or other heart and non-heart diseases that cause chest pain and high blood pressure (19). Copeptin is elevated in critical illnesses associated with hypovolemia or hypotension. This is believed to be due to the increased secretion of AVP, which is stimulated by hypovolemia. Studies have also shown that in patients with refractory hypertension, after adjusting for plasma osmolality, plasma copeptin concentrations were approximately

twice as high as in patients with CBP. Indicating an initial reset of osmostat (21, 20). copeptin as a new biomarker can be used to diagnose various diseases and predict functional consequences. Because it is not particular to a specific disease, it can be used as a sub-biomarker alongside specific biomarkers that may increase the accuracy of the diagnosis and help clinicians make better diagnoses. However, copeptin is still incomplete and further studies are needed to demonstrate its clinical use.

References

1. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. European Heart J 2018;39(33):3021-104.
2. Griendling, K. K., Camargo, L. L., Rios, F. J., Alves-Lopes, R., Montezano, A. C., & Touyz, R. M. (2021). Oxidative stress and hypertension. Circulation Research, 128(7), 993-1020.
3. Dokunmu TM, Yakubu OF, Adebayo AH, Olasehinde GI, Chinedu SN. Cardiovascular Risk Factors in a Suburban Community in Nigeria. Int J Hypertens. 2018; 2018: 6898527.
4. Tian, Z., & Liang, M. (2021). Renal metabolism and hypertension. Nature Communications, 12(1), 1-12.
5. Galindo Yllu, B. M. (2022). Copeptin and metabolic syndrome: a systematic review.
6. Morgenthaler NG, Struck J, Alonso C, Bergmann A. Assay for the measurement of copeptin, a stable peptide derived from the precursor of vasopressin. Clin Chem. 2006;52:112-9.
7. Zang, J., Liu, A. X., & Qi, L. (2019). The cytological mechanism and effects of hypertensive cerebral hemorrhage treatment by citicoline on serum GFAP and copeptin level. European Journal of Inflammation, 17, 2058739219867244.
8. Enhörning S, Struck J, Wurfält E, Hedblad B, Morgenthaler NG, Melander O (2011) Plasma copeptin, a unifying factor behind the metabolic syndrome. J Clin Endocrinol Metab 96(7):E1065–E1072.
9. Enhörning S, Bankir L, Bouby N, Struck J, Hedblad B, Persson M, Morgenthaler NG, Nilsson PM, Melander O (2013) Copeptin, a marker of vasopressin, in abdominal obesity, diabetes and microalbuminuria: the prospective malmö diet and cancer study cardiovascular cohort. Int J Obes 37(4):598–603.
10. Przybylowski P, Malyszko J, Malyszko JS (2010) Copeptin in heart transplant recipients depends on kidney function and intraventricular septal thickness. Transplant Proc 42(5):1808–1811.
11. Li X, Yang XC, Sun QM, Chen XD, Li YC (2013) Brain natriuretic peptide and copeptin levels are associated with cardiovascular disease in patients with chronic kidney disease. Chin Med J (Engl) 126(5):823–827.
12. Ray, P., Charpentier, S., Chenevier-Gobeaux, C., Reichlin, T., Twerenbold, R., Claessens, Y. E., ... & Mueller, C. (2012). Combined copeptin and troponin to rule out myocardial infarction in patients with chest pain and a history of coronary artery disease. The American journal of emergency medicine, 30(3), 440-448.
13. Engelbertz C, Brand E, Fobker M, Fischer D, Pavenstädt H, Reinecke H. Elevated copeptin is a prognostic factor for mortality even in patients with renal dysfunction. Int J Cardiol. 2016;221:327–32.
14. Bhandari SS, Loke I, Davies JE, Squire IB, Struck J, Ng LL. Gender and renal function influence plasma levels of copeptin in healthy individuals. Clin Sci(Lond). 2009;116:257–63.
15. Meijer E, Bakker SJ, Halbesma N, de Jong PE, Struck J, Gansevoort RT. Copeptin, a surrogate marker of vasopressin, is associated with microalbuminuria in a large population cohort. Kidney Int. 2010;77:29–36.

16. Schoen T, Hohmann EM, Van Der Lely S, Aeschbacher S, Reusser A, Risch M, Risch L, Conen D. Plasma copeptin levels and ambulatory blood pressure characteristics in healthy adults. *J Hypertens.* 2015;33:1571-9.

17. Tenderenda-Banasiuk E, Wasilewska A, Filonowicz R, Jakubowska U, Waszkiewicz-Stojda M. Serum copeptin levels in adolescents with primary hypertension. *Pediatr Nephrol.* 2014;29:423-9.

18. Mendes M, Dubourg J, Blanchard A, Bergerot D, Courand PY, Forni V, Frank M, Bobrie G, Menard J, Azizi M. Copeptin is increased in resistant hypertension. *J Hypertens.* 2016;34:2458-64.

19. Zhong, Y., et al. (2017). "Copeptin in heart failure: Review and meta-analysis." *Clinica Chimica Acta* 475: 36-43.

20. Mendes, M., Dubourg, J., Blanchard, A., Bergerot, D., Courand, P. Y., Forni, V., ... & Azizi, M. (2016). Copeptin is increased in resistant hypertension. *Journal of hypertension*, 34(12), 2458-2464.

21. Sahin, I., Gungor, B., Ozkaynak, B., Uzun, F., Küçük, S. H., Avci, I. I., ... & Dinckal, M. H. (2017). Higher copeptin levels are associated with worse outcome in patients with hypertrophic cardiomyopathy. *Clinical cardiology*, 40(1), 32-37.