



Study of Serum Copeptin Levels in Newly Diagnosed Hypothyroid Subjects

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ABSTRACT

Introduction: Hypothyroidism is one of the most commonly occurring thyroid disorders worldwide. Hypothyroidism is due to decreased circulating levels of thyroid hormones and is caused by inadequate functioning of the thyroid gland. Copeptin (CPP), the C-terminal part of the vasopressin prohormone, is released stoichiometrically with arginine-vasopressin from the neurohypophysis and seems to reflect the individual endogenous stress level and also the mortality risk in coronary events. This study aimed to determine Copeptin levels in hypothyroidism and to evaluate the relationship between CPP and thyroid hormone levels. **Methodology:** The present study was conducted on 80 newly diagnosed hypothyroid subjects attending the Medical OPD and Immunoassay Laboratory of the Department of Biochemistry, S.P. Medical College and Hospitals, Bikaner. The results of patients were compared with 80 healthy controls of either sex of a similar age group (20-65 years). The blood samples were collected from all the subjects and analyzed for serum thyroid profile and CPP. The thyroid profile was estimated by the electro-chemiluminescence system, using an automated Beckman coulter immunoassay analyzer. Cpp was estimated by Elisa kit using Merilyzer. **Results:** The mean serum CPP level was observed statistically highly significant ($p < 0.001$) in hypothyroid subjects (192.71 ± 58.68 pg/ml) as compared with healthy control subjects (51.28 ± 11.37 pg/ml). A highly significant positive correlation was found (+0.89) between CPP with TSH ($p < 0.001$) and significant negative correlations were found between CPP with T3 and T4 in hypothyroid subjects. **Conclusion:** CPP levels in hypothyroid subjects might be useful as an early marker to detect future cardiac and endothelial diseases

Keywords: Hypothyroidism, Total T3, Total T4, TSH, Copeptin

INTRODUCTION

Hypothyroidism is known to be one of the most common endocrine disorders resulting from insufficient production or impaired action of thyroid hormone. Thyroid hormones facilitate the normal growth and function of nearly all the tissues with a prominent effect on oxygen consumption. Thyroid hormone plays an important role in cell differentiation and helps to maintain metabolic homeostasis in the body; its alteration can affect the metabolism and can alter the activity of serum enzymes. Thyroid Stimulating Hormone (TSH) is a very sensitive and specific parameter to assess thyroid function and has importance in early detection or exclusion of thyroid disorder [1,2]. Copeptin (CPP), a novel biomarker that has entered the clinical era, was found to be a stable and sensitive surrogate marker for Arginine Vasopressin (AVP) [3]. Copeptin is a 39-aminoacid glycopeptide, which is a stable COOH-terminal part of the precursor pre-vasopressin and concealing a leucine-rich core segment, It is a neurohormone of the AVP system, that is secreted in an equimolar ratio to AVP from the hypothalamus [4,5]. It is also called AVP-connected glycopeptide and was primarily designated by Hollwerda in 1972 [6]. Copeptin, the C-terminal part of the vasopressin prohormone, is released stoichiometrically with arginine-vasopressin from the neurohypophysis and seems to reflect the individual endogenous stress level and also the mortality risk in coronary events [7]. Copeptin has been correlated with endothelial function in humans [8].

MATERIALS AND METHODS

The present study was conducted on 80 newly diagnosed hypothyroid subjects attending the Medical OPD and Immunoassay Laboratory of the Department of Biochemistry, S.P. Medical College and Hospitals, Bikaner. The

results of patients were compared with 80 healthy controls of either sex of a similar age group between 20-65 years. The diagnosis of hypothyroidism was established, based on the clinical signs and symptoms and the T3, T4, and TSH estimations (American Thyroid Association). For the control group, age and sex-matched healthy volunteers were selected. Patients on treatment for any thyroid disorder, liver disease, and lipid-lowering drugs, diabetes, malignancy, and pregnant women were excluded. The study was approved by the Ethics committee of our college. Informed consent was taken from all the study subjects. All the anthropometric measurements were performed. Blood sample collection was done by aseptic technique and subjected to biochemical estimations. The thyroid profile was estimated by the electro-chemiluminescence system, using an automated Beckman coulter immunoassay analyzer. Cpp was estimated by Elisa kit using Merilyzer. p-values <0.05 were considered significant.

RESULTS

The Mean \pm SD levels of serum T3, T4, TSH, and CPP were highly significant ($p < 0.001$) in hypothyroid subjects as compared with healthy control subjects (Table 1). Serum CPP showed a highly significant positive correlation ($p < 0.001$) with TSH and significant negative correlations ($p < 0.05$) with T3 and T4 in the hypothyroid subjects (Table 2).

Table 1 Comparison of parameters of the subjects studied; ** $p < 0.001$ =Highly Significant (HS).

S. No.	Parameters	Controls (Mean \pm SD)	Hypothyroid subjects (Mean \pm SD)	p-value
1	Serum T3 (ng/ml)	1.27 \pm 0.30	0.66 \pm 0.31	$p < 0.001$ (HS)
2	Serum T4 (μ g/dl)	9.23 \pm 2.29	3.75 \pm 1.94	$p < 0.001$ (HS)
3	Serum TSH (μ IU/ml)	2.46 \pm 1.12	25.61 \pm 15.60	$p < 0.001$ (HS)
4	CPP (pg/ml)	51.28 \pm 11.37	192.71 \pm 58.68	$p < 0.001$ (HS)

Table 2 Correlation of CPP with thyroid profile in hypothyroidism; * $p < 0.05$ =Significant (S); ** $p < 0.001$ =Highly Significant (HS)

Parameters	Correlation (r)	p-value
T3 vs. CPP	-0.67	$p < 0.05$ (S)
T4 vs. CPP	-0.62	$p < 0.05$ (S)
TSH vs. CPP	+0.89	$p < 0.001$ (HS)

DISCUSSION

Hypothyroidism is a common metabolic disorder in the general population. It is associated with increased morbidity from cardiovascular disorder. CPP, the C-terminal portion of pre-pro AVP, is a polypeptide comprising 39 amino acids. It is a neuro-hormone of the AVP system that is co-secreted with AVP from the hypothalamus. Copeptin has recently come into clinical practice and has been regarded as a novel neuro-hormone [5]. Our results showed significantly higher levels of serum CPP in hypothyroid patients as compared with euthyroid controls. This rise in serum CPP level, though evident in the hypothyroid group. Following the current results, Skowsky and Kikuchi showed that plasma AVP was elevated in patients with hypothyroidism [9]. Similarly, Nakano, et al. have noted the augmentation of antidiuretic hormone levels in the state of hypothyroidism and reported that patients with hypothyroidism showed hyponatremia and elevated plasma vasopressin without hypovolemia, and laboratory findings and the clinical signs were similar to a syndrome of inappropriate antidiuretic hormone secretion [10]. In support of the associations between CPP and thyroid hormones, the correlation coefficient (Table 2) showed a significant positive correlation between increased CPP and elevated TSH levels in hypothyroid subjects. Besides, there were negative correlations of CPP with T3 or T4 in these subjects. These results indicate that hormonal disturbances are associated with increased oxidative stress status in hypothyroid patients. Therefore, we also considered studying and report the effect of normalizing thyroid status on serum CPP levels in hypothyroid cases. Our study confirmed that the estimation of CPP would be helpful in the early diagnosis of cardiac and endothelial diseases. This may help in preventing the chances of irreversible infarction in patients with altered levels of thyroid hormones.

CONCLUSION

Copeptin levels in hypothyroid subjects might be useful as an early marker to detect future cardiac and endothelial diseases.

DECLARATIONS

Conflicts of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

- [1] Meier, Christian, et al. "Serum thyroid stimulating hormone in assessment of severity of tissue hypothyroidism in patients with overt primary thyroid failure: Cross sectional survey." *BMJ*, Vol. 326, No. 7384, 2003, pp. 311-12.
- [2] Kaur, Navreet, Sukhraj Kaur, and Mridula Mahajan. "Correlation of thyroid hormones with lactate dehydrogenase activity." *International Journal of Current Research*, Vol. 8, No. 6, 2016, pp. 32616-18.
- [3] Llorens, Pere, et al. "The utility of copeptin in the emergency department for non-ST-elevation myocardial infarction rapid rule out: COPED-MIRRO study." *European Journal of Emergency Medicine*, Vol. 21, No. 3, 2014, pp. 220-29.
- [4] Voors, Adriaan A., et al. "C-terminal pro vasopressin (copeptin) is a strong prognostic marker in patients with heart failure after an acute myocardial infarction: Results from the OPTIMAAL study." *European Heart Journal*, Vol. 30, No. 10, 2009, pp. 1187-94.
- [5] Morgenthaler, Nils G., et al. "Copeptin: Clinical use of a new biomarker." *Trends in Endocrinology and Metabolism*, Vol. 19, No. 2, 2008, pp. 43-49.
- [6] Holwerda, Dirk A. "A Glycopeptide from the Posterior Lobe of Pig Pituitaries: 1. Isolation and Characterization." *European Journal of Biochemistry*, Vol. 28, No. 3, 1972, pp. 334-39.
- [7] Mueller, Christian. "Biomarkers and acute coronary syndromes: An update." *European Heart Journal*, Vol. 35, No. 9, 2014, pp. 552-56.
- [8] Schnabel, Renate B., et al. "Multiple endothelial biomarkers and non-invasive vascular function in the general population: The Gutenberg Health Study." *Hypertension*, Vol. 60, No. 2, 2012, pp. 288-95.
- [9] Skowsky, W. Ronald, and Thomas A. Kikuchi. "The role of vasopressin in the impaired water excretion of myxedema." *The American Journal of Medicine*, Vol. 64, No. 4, 1978, pp. 613-21.
- [10] Nakano, Masatsugu, et al. "Hyponatremia with increased plasma antidiuretic hormone in a case of hypothyroidism." *Internal Medicine*, Vol. 39, No. 12, 2000, pp. 1075-78.