Original Research Article **Physiology**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

URINARY C-PEPTIDE AND URINE C-PEPTIDE/CREATININE RATIO (UCPCR) ARE POSSIBLE PREDICTORS OF ENDOGENOUS INSULIN SECRETION IN T2DM SUBJECTS - A RANDOMIZED STUDY

KULKARNI C M[1], SUMANGALA PATIL[2].

[1]Associate Professor, Department of Physiology, B.L.D.E.University's Shri B.M.Patil Medical College,Bijapur,Karnataka, India.
[2]Professor, Department of Physiology, B.L.D.E.University's Shri B.M.Patil Medical College,Bijapur,Karnataka, India.

ABSTRACT

Estimation of serum C-peptide (SCP) is used as a measure of endogenous insulin secretion in type 2 diabetes mellitus (T2DM). Urinary C- Peptide (UCP) and urinary C-Peptide creatinine ratio (UCPCR) are non invasive, simple and easily reproducible tests which may be considered as an alternative for SCP. In our study we estimated fasting serum C-peptide, urinary C-peptide and UCPCR in Type 2 Diabetes Mellitus (T2DM) subjects (n=113; male=74; female=39) with normal serum creatinine and urea levels. In all the cases of T2DM significant correlation were observed between serum C-peptide to urinary C-peptide and UCPCR. A significant correlation between serum C-Peptide and urinary C-Peptide in males and a significant correlation between serum C-Peptide and UCPCR in female subjects were also noticed. In T2DM subjects' estimation of UCP in males and UCPCR in females may be used as simple, reproducible tests as predictors/biomarkers of endogenous insulin levels to assess status of beta cell functions.

KEY WORDS: **Serum C-peptide,Urinary C-peptide, Urinary C-peptide Creatinine Ratio, type 2 diabetes mellitus**

KULKARNI C M
Associate Professor,Department of Physiology, B.L.D.E.University's Shri B.M.Patil Medical College,Bijapur,Karnataka, India

***Corresponding Author**

INTRODUCTION

C peptide is produced by a series of enzymatic cleavages of the precursor molecules pre proinsulin and proinsulin. Proinsulin is the precursor of insulin and C-peptide.[1] Insulin is produced in the pancreatic beta cells by enzymatic cleavage of the prohormone precursor proinsulin to insulin and C-peptide in equimolar amounts. C-peptide has negligible extraction by the liver and constant peripheral clearance. Its plasma half life is longer than insulin (20-30 vs 3-5 min) and It circulates at 5 times higher concentration than insulin in systematic circulation. C-peptide is commonly used in preference to insulin measurement to assess beta cell function in clinical practice. Insulin produced by the pancreas is extensively metabolized by the liver (50%), both the extent of first pass metabolism and peripheral clearance of insulin is variable. So peripheral insulin levels may not accurately reflect portal insulin secretion. Even in non insulin treated patients, peripheral C-peptide levels reflect more portal insulin secretion than of peripheral insulin. Approximately half of C-peptide is removed by the kidneys, majority of which is degrade via peritubular uptake with approximately 5% of total C-peptide produced is excreted unchanged in the urine[2]. Clinical diagnosis of T2DM usually made but subsequent development of absolute insulin deficiency is rarely tested or suspected. Urine C-peptide measurement is a potentially attractive noninvasive measure of beta cell function[3]. C-peptide is excreted in the urine through glomerular filtration and uptake from peritubular capillaries. Simple urine estimation of C-Peptide and urine C-Peptide creatinine ratio (UCPCR) can be an excellent test to measure endogenous insulin secretion instead of measuring serum C-Peptide[2]. Thus C-peptide measurements seem to represent a better alternative index of insulin secretion and residual β-cell function[4]. Hence present study is undertaken to compare and correlate urinary C-Peptide, UCPCR with serum C-Peptide in T2DM in both sex and feasibility, accuracy of estimation of UCP and UCPCR.

MATERIALS AND METHODS

This was a cross sectional study conducted during the year 2012-13, A total of 113 (≥40 years) Type 2 diabetes patients of either sex (males no=74 and females no=39) without renal impairment were included in the study. Type 2 diabetic patients with established renal impairment and who are on insulin therapy were excluded from the study. Institutional Ethics Committee (IEC) clearance was taken from institution and informed consent was obtained from all subjects. Subjects were selected randomly as they attend Diabetes outpatient department (OPD) in B M Pail Medical College Hospital and Research Centre. Fasting blood and urine samples were collected at 9 am from the participants at the time of their routine OPD visit. In blood samples Fasting blood sugar, serum C-peptide (SCP), serum creatinine and blood urea levels were estimated. From the urine samples, urine creatinine, urinary C-peptide (UCP) levels were estimated and Urinary C-peptide/creatinine ratio (UCPCR) was calculated. Estimation of fasting blood sugar (FBS) was done by using Easy Glucometer. C-peptide estimation was done by using chemiluminiscence assay method with kits.

STATISTICAL ANALYSIS

Statistical was done using SPSS version 20. The results were expressed as Mean ± SD. Correlation was done with spearman correlation coefficient. $P<0.05$ was considered as statistically significant.

RESULTS

Table-I shows spearman correlation study between serum C-peptide and other parameters such as age, serum creatinine, blood urea, urine creatinine, urinary C-peptide, UCPCR and plasma glucose levels. It clearly showed significant correlation between serum C-peptide and age (p=0.000), c-peptide and serum creatinine (p=0.006), SCP and blood urea (p=0.002), SCP and UCPCR (p=0.041) in female subjects of T2DM. There was no significant correlation between serum C-peptide and urinary C-peptide as observed in male subjects.

Table 1
Spearman Correlation coefficient of total Female subjects between C-peptide and other variables (n=39)

	Variables(n=39)	(r-value)	p value
1	Age	0.439	0.000*
2	Serum Creatinine (mg/dL)	0.270	0.006*
3	Blood Urea (mg/dL)	0.308	0.002*
4	Urinary C- Peptide (ng/mL)	0.150	0.319
5	Urine Creatinine (mg/dL)	-0.057	0.707
6	Urine C-peptide/ Creatinine Ratio	0.302	0.041*
7	FBS (mg/dL)	0.184	0.063

Note: *: significant as p<0.05

Table-2 shows spearman correlation study between serum C-peptide and other parameters such as age(p=0.208), serum creatinine(p=0.444), blood urea(0.234), urine creatinine(0.333), and urinary C-peptide, UCPCR and plasma glucose levels. It clearly shows significant correlation between C-peptide and urinary C-peptide (p=0.006) in male subjects of T2DM.This difference is due to difference in muscle mass and creatinine excretion.

Table 2
Spearman Correlation coefficient of total male subjects between C-peptide and other variables (n=74)

	Variables(n=74)	r- value	p value
1	Age	0.113	0.208
2	Serum Creatinine (mg/dL)	0.069	0.444
3	Blood Urea (mg/dL)	0.106	0.234
4	Urinary C- Peptide (ng/mL)	0.241	0.006*
5	Urine Creatinine (mg/dL)	0.087	0.333
6	Urine C-peptide/ Creatinine Ratio	0.113	0.207
7	FBS (mg/dL)	-0.066	0.462

Note: * significant as p<0.05

DISCUSSION

In our study in male subjects we observed that there is significant correlation between serum C-peptide (SCP) and urinary C-peptide(UCP) which coincided with study of AG Jones[5]. Urine C-Peptide (UCP) measurement is a potentially attractive noninvasive measure of beta cell function of pancreas. Total quantity of C-Peptide excreted in urine per day represents 5% of pancreatic secretion as to only 0.1% of secreted insulin. Correcting for creatinine adjusts UCP concentration for variation in urine. This helps the use of spot urine samples instead of 24 hour urine collection. UCPCR levels are found to be 1.5 times higher in women than men, due to higher creatinine levels in men[6]. Whereas female subjects showed significant correlation between serum C-peptide (SCP) and serum creatinine, blood urea and urinary C-peptide/creatinine ratio (UCPCR). Our study also supports the observations of UCPCR as a noninvasive outpatient tool to differentiate between maturity onset diabetes of young (MODY), Type 1 Diabetes Mellitus (T1DM) and T2DM[7]. Study also found a strong correlation of UCPCR and serum C peptide in mixed meal tolerance test(MMTC) which indicated that timed measures of UCP are useful marker of endogenous insulin secretion. These observations partially correlate with our observations and suggestive of UCPCR as a potential biomarker in clinical practice to assess T2DM, similar observations were found by Besser RE et al[8] in T1DM and Bowman P et al[9] in T2DM. Studies also revealed that SCP and UCPCR can distinguish between MODY and T1DM with high specificity and sensitivity which once again partially support our observations that SCP and UCPCR correlates only in females, whereas SCP and UCP correlates with male subjects[10]. Further it may be concluded that the urinary C-peptide creatinine ratio is a practical non-invasive method to aid detection of absolute insulin deficiency. A urinary C-peptide creatinine ratio > 0.2 nmol/mmol indicates retained endogenous insulin secretion[11]. The reason behind the higher creatinine excretion in male in our study may be due to higher muscle mass and creatinine production and with higher protein metabolism in muscles[12].

CONCLUSION

It may be concluded that in normal to moderate impairment of renal function estimation of UCP in males and UCPCR in females are probably good predictors/biomarkers of beta cell function or endogenous insulin secretion of pancreas in T2DM subjects.

Limitations and future scope of the study

This is a hospital based study and only subjects (both sexes) attending diabetes OPD were included in study. Sample size is small and further study involving large sample size will probably throw more light on this study. Further study is required for standardization of normal levels of urinary C-peptide in different ethnic population.

ACKNOWLEDGMENT

Authors would like to express deep gratitude and thanks to Vice Chancellor, Registrar, Principal and Dean Faculty of Medicine, Professor K. K Das and Professor and HOD Dr. Manjunath A, Department of Physiology of BLDE University's Shri B M Patil Medical College, Vijayapura, Karnataka for their Constant inspiration and support. I am extremely grateful to all subjects for their active participation and cooperation. Authors are very much thankful to all authors/ editors/publishers of all those articles, journals and books reviewed and discussed in this article.Financial support and sponsorship BLDE University Vijaypur, Karnataka.

CONFLICT OF INTEREST

Conflict of interest declared none.

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