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PROTEIN METABOLITES; (CREATININE & UREA)
ELIMINATION THROUGH KIDNEYS IN HEALTHY FEMALES

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ABSTRACT ... sa_husain@hotmail.com The elimination of blood and urinary levels of creatinine and urea, were determined in healthy volunteers who were on normal diet. **Setting:** University of Agriculture, Faisalabad. **Objectives:** The present study was aimed at analyzing the renal elimination of endogenous creatinine and urea in healthy females to establish a base line data for the local population. **Materials & Methods:** The blood and urine samples of 8 healthy female subjects, collected at appropriate time intervals, were retained for the determination of endogenous creatinine and urea in them, spectrophotometrically. **Results & Discussion:** The mean ± SD concentration of creatinine in plasma of healthy female volunteers was 9.23± 2.54 µg/ml and in urine 374.08±489.90 µg/ml. Whereas, concentration of urea in plasma was 290.46± 107.27 µg/ml and in urine 27172.80± 4338.45 µg/ml. Creatinine renal clearance was 0.81± 0.49 ml/min/kg (range 0.15-1.18) and urea clearance 9.11± 0.11 ml/min/kg (range 0.04-0.26). These values existed within the normal range as described in the literature, but a bit lower than values given in the foreign literature. **Conclusion:** Creatinine and urea levels in the body are relatively stable. These remain unchanged unless there is sudden deterioration in renal function.
Key Words: Protein metabolites, endogenous creatinine and urea, renal clearance, GFR, female volunteers.

INTRODUCTION

Proteins are one of the most abundant components of human body and occupy a central position in the architecture and functioning of living matter.[1] The dietary and intracellular proteins in the body are metabolized into their building blocks, amino acids. Three amino acids arginine, glycine and methionine are metabolized to form creatine which is primarily a high energy phosphate compound utilized for muscular contraction.[2]

Creatine is ultimately converted into creatinine, a waste product in the blood that is created by the normal breakdown of muscles during physical activity[3].Free creatinine occurs in both blood and urine and is completely filtered at the glomerulus, not reabsorbed in the tubules and is excreted almost entirely and unchanged in the urine. Its blood concentration increases when kidneys are not functioning. Hence, creatinine clearance is the best measure of glomerular filtration rate (GFR)[4]. Urea is a metabolic by-product of protein-rich foods and a major organic component of human urine. It is synthesized from ammonia in liver and excreted by kidneys.[5]

Blood urea nitrogen varies directly with protein intake. Due to tubular reabsorption of urea, only 46% of urea is excreted so it is less useful measure of GFR than creatinine.[6] If the kidneys are suddenly unable to function, urea and creatinine levels are increased in the blood.[7] Since information about the renal elimination of protein metabolites in the local population is scanty, therefore, this project was designed to analyze the renal handling of endogenous creatinine and urea in healthy females to establish the baseline data.

MATERIALS & METHODS

The study was performed by taking blood and urine samples at specific time interval. The volume of urine, pH of urine and fresh blood was determined and the plasma was separated out. The concentrations of endogenous creatinine and urea were estimated in blood and urine by analytical methods and then renal clearance of these metabolites was determined. The human clinical study protocols were strictly observed.

Volunteers:

The elimination of protein metabolites, endogenous creatinine and urea, were investigated in 8 healthy female volunteers with mean age of 20 years, body weight 50 kg and height 158 cm. The volunteers had already been apprised of the study protocols and a written consent form was also signed by all of them.

Sampling:

The blood samples were drawn, at specific intervals, from the arm vein with a 5 ml sterilized syringe by inserting a cannula into it. The heparinized blood samples were centrifuged at 4000 rpm for 10 minutes to separate plasma to be kept in closed tubes at-20°C till analysis. The urine samples were also collected between the sampling of blood. The volume of urine at each sampling time was measured and was preserved in a freezer, maintained at -20°C.

Biochemical Analysis:

The creatinine was estimated by Jaffe's Reaction[8] in which alkaline pirate reacted with creatinine in the plasma and urine producing a golden yellow color, the intensity of which was measured at 515 nm. The concentration of urea in the plasma and urine was determined by End point-Berthelot reaction,[9] in which ammonium ions reacted with a mixture of salicylate, hypochlorite and nitroprusside to yield a blue-green dye (indophenol). The color intensity was measured spectrophotometrically at 578nm.

Statistics:

The data were recorded, tabulated and the calculations were done according to the standard methods. Mean±SD, maximum and minimum values were calculated for creatinine and urea using Microsoft Excel Software. The correlation between the urine volume, pH and plasma concentrations of

endogenous creatinine and urea and its renal clearance were determined by means of regression/correlation analysis[10].

RESULTS & DISCUSSION

There is more creatinine in the urine of children than adults, whereas men excrete less than women, Besides the gender, urinary creatinine is also dependent on age, muscle mass and amount of meat taken in the diet[11]. Creatinine coefficient is, therefore, higher in individuals with an increased muscle mass and lower in obese individuals[12]. A high protein intake, vigorous muscular exercise and pregnancy tend to increase, and rneal insufficiency decrease the creatinine clearance moderately[13]. Creatinine clearance is also age related. In old age the decline of creatinine is due to less production of creatinine, as muscle mass decline with the age and only minimally dependent on physical activity, protein intake and protein catabolism [14].

Table-I. Mean ± SD values of creatinine and urea with renal clearance in the volunteers.

Values	Creatinine Concentration (µg/ml)		Urea Concentration (µg/ml)		Renal Clearance (ml/min/kg)	
	Plasma	Urine	Plasma	Urine	Creatinine	Urea
Mean	9.23	374.08	290.46	27172.80	0.81	0.11
Maximum	13.35	719.92	353.33	31674.13	1.18	0.26
Minimum	6.28	102.49	256.67	23313.97	0.15	0.04
SD	2.54	489.90	107.27	4338.45	0.49	0.11

Urea clearance vary with the urine flow[15]. Whereas, blood urea nitrogen varies directly with protein intake which is lowered by fasting and inversely with rate of excretion of urea. Further, blood urea level remains unchanged unless there is sudden deterioration of renal function. Also, plasma urea is inversely related to clearance, it increase in dehydration and its synthesis is increased in protein breakdown[16]. Decrease in urea level may be due to liver dysfunction[17].

In the present study, as table 1 reveals, mean±SD concentration of creatinine in plasma of healthy female volunteers was 9.23±2.54 ug/ml and in urine 374.08±489.90 ug/ml. Whereas, concentration of urea in plasma was 290.46±107.27 ug/ml and in urine 27172.80±4338.45 ug/ml. Creatinine renal clearance was 0.81±0.49 ml/min/kg (range 0.15-1.18) and urea clearance 0.11±0.11 ml/min/kg (range 0.04-0.26). These values existed within the normal range but a bit lower than values given in the cited foreign literature. This may be due to the reason that foreign people have better nutritional status with more muscle mass than people here in Pakistan.

The study indicates that the amounts of creatinine and urea produced in the body are relatively stable and remain unchanged unless there is sudden deterioration of renal function.

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