EFFECTS OF HEMODIALYSIS ON THE ESTIMATED LEVEL OF UROTENSIN II IN CHRONIC RENAL FAILURE MALE PATIENTS IN ERBIL CITY

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Abstract

Background and objectives: Human urotensin II (UII) is a potent mammalian vasoconstrictor thought to be produced and cleared by the kidneys. Conflicting data exist regarding the relationship between UII concentrations, kidney function and blood pressure (BP). We examined the effects of hemodialysis on the plasma level of urotensin II concentrations in chronic renal failure male patient.

Methods: In this study, 40 male patients on maintenance hemodialysis were enrolled. We estimated the urotensin II concentrations by the ELISA method. We compared the urotensin II concentrations before and after hemodialysis for each patient, using paired t-test.

Results: The effects of hemodialysis on the urotensin II concentrations were statistically non-significant as the p value was >0.05, (p=0.6983), but we found that the hemodialysis has a statistically significant effects on the Glomerular Filtration Rate (GFR), blood urea, serum creatinine, systolic blood pressure (SBP) and diastolic blood pressure (DBP), with p value of (0.0330, 0.0001, 0.0001, 0.0001, 0.0001), respectively. It has been found that the urotensin II is correlated positively with both blood urea and serum creatinine and correlated negatively with SBP and DBP, although these correlations were statistically not significant.

Conclusion: These results suggest that the hemodialysis has no significant effects on the urotensin II concentrations before and after HD, but we found that the HD has a statistically significant effect on SBP or DBP and on renal functions.

Keywords: Urotensin II; Chronic Renal failure.

Introduction

UII is one of the most potent vasoconstrictors in mammals.[1-3] Although both UII and its receptor, G protein coupled receptor-14 (GPR14), are detected in several tissues, kidney is a major source of UII in humans.[4-7] It's suggested that U-II may have a possible autocrine/paracrine functions in kidney and may be an important target molecule in studying renal pathophysiology.[2] It has several effects on tubular transport and probably has active role in renal hemodynamics.[7-9] It is an important peptide in renal physiology, certain diseases, such as hypertension and glomerulonephritis, Alter the expression of UII.[1] UII is a potent mammalian vasoconstrictor thought to be produced and cleared by the kidneys.[1] Conflicting data exist regarding the relationship between UII concentrations, kidney function and blood pressure (BP).[2] The urotensins are a family of vasoactive peptides first isolated from various fish species nearly 40 years ago and later from frogs, rodents, pigs, primates and humans.[3] The vasomotor effects of UII vary greatly, depending on the species studied, interactions with other vasoactive molecules and the vascular bed used. [9-12] The kidney plays a major role in UII production, which may contribute to its hemodynamic effects.[12-15] UII can also be synthesized in non-renal tissue, such as the heart.[4] Some researchers have shown that UII may play a cardioprotective role in patients with ischemic heart disease and CRF.[3] Several studies have shown increased UII levels in patients with chronic kidney disease (CKD).[2] Some investigators implicate UII in the pathophysiology of many diseases including CKD.[15,16] Previous studies have shown an increase in the UII levels in patients with CKD, including those undergoing HD.[5] Increased levels of UII were noticed in Plasma from patients with renal failure (2 ± 3 fold greater than control), with those on dialysis recording the highest concentrations.[5] The increased plasma UII in renal failure patients may reflect reduced clearance by the kidneys, but increased production of UII in disease cannot be discounted.[6] This study aimed to examine the effect of HD on the plasma level of UII in CKD patients.

Methods

The study was conducted in Erbil city during July and August 2015. A sample of 40 adult male patients with CRF on maintenance hemodialysis in Hawler dialysis center, Hawler teaching hospital was included in the study. The UII level was estimated for each patient before and after HD. We classified our patients into several groups which include: hypertensive and non-hypertensive, diabetic and non-diabetic, those taking calcium channel blocker and those not taking calcium channel blocker, and then we compared the level of UII before and after HD for each group. Also, we classified our patients according to their body mass index (BMI) into the following groups: underweight those with BMI of <18.5, normal weight those with BMI=18.5-24.9, overweight those with BMI=25-29.9, obese those with BMI=30-39.9, then we compared the UII level before and after HD for each group. Height and weight of the participants were measured before hemodialysis using a portable stadiometer from Seca- USA and digital weight scale from Seca-USA. BMI was calculated using the formula: Weight (Kg) /Height (square meter)(WHO, 2008). BP was recorded for every participant before and after HD using a mercury sphygmomanometer from morningside pharmaceuticals-UK. Inclusion criteria included all male patients on maintenance HD. Exclusion criteria included females, children and smoker patients.

This study was a part of MSc thesis and the study proposal was approved by both the scientific and the ethical committee of the College of Medicine, Hawler Medical University, Erbil, Kurdistan region, 2015-2016.

A sample of 5 ml of venous blood were taken from each patient before and after HD, the blood was withdrawn from any accessible vein, About 3 ml of each blood sample was rapidly placed in a vacuum blood collection tube containing (anticoagulant-EDTA), from unimedica-Jordan, centrifuged immediately for 20 minutes at room temperature at 3000rpm using (Tomy GRX-high speed centrifuge, Tokyo, Japan). The plasma was separated and stored in a flat- bottom blood collection tube with screw cap with no anticoagulant from citotest-China at -20 - 80 celsius and assayed a week later for the estimation of human UII hormone. The remaining 2 ml of the blood samples were placed in serum separator tubes (clot activator tube) from AFCO- Jordan, left aside for 20 minutes to clot and centrifuged for 15 minutes at 3000rpm

using Labofuge 200 centrifuge-Germany.The separated serum was used for biochemical analysis of (Creatinine, Urea and Electrolytes).

Measurement of plasma UII was done using human UII ELISA kit from Thermoscientific-USA. The whole procedure was carried out in Nanakaly hospital in Erbil city using Bio-Tek® microplate reader and Bio-Tek® automatic microtiter plate washer-USA. All the steps in the preparation of the samples and standards and the measurement procedures were according to the procedure provided by the manufacturer. The measurement of blood urea, serum electrolyes and serum creatinine were carried out in the laboratory of dialysis center at Komary hospital in Erbil city. The Cockroft–Gault equation was used for the estimation of the GFR. The data was analyzed using the GraphPad Prism 6.01 for windows. All the data are expressed as mean, standard deviation (SD) and/or standard error (SE). Statistical analysis was used according to the paired t- test for comparing the samples. Pearson's correlation coefficient was also used to correlate the measured parameters. A P-value of 0.05 or less was considered to be statistically significant.

Results:

Socio-demographic informations of the participants

The socio-demographic information of the participants are shown in (Table 1), the majority of our participants were old age, age group ranging between (60-69.9 yrs), most of them with normal BMI (BMI=18.9-24.9) and most of them were hypertensive (25 out of 40 patients).

Table 1: Socio-demographic information of the participants

Variable	No.	%
No of patients	40	100
Male	40	100
Female	0	0.0
Smoker	0	0.0
Non-smoker	40	100
Age group in years		
20-29.9	3	7.5
30-39.9	7	17.5
40-49.9	5	12.5
50-59.9	9	22.5
60-69.9	13	32.5
70-79.9	3	7.5
BMI		
Less than 18.5	4	10
18.5-24.9	18	45
25-29.9	10	25
30-39.9	7	17.5
More than 40	1	2.5
Diabetic	15	37.5
Hypertensive	25	62.5

Estimation ofUII:

In this study the level of UII was estimated for each patient before and after HD using paired t-test of the same sample, the result was statistically non-significant as the p value was > 0.05 (Table 2 and figure 1), the GFR, blood urea and serum creatinine were also estimated for each patient before and after HD using paired t-test for the same sample and the results were statistically highly significant as the p value was > 0.05 (Table 2 and figure 2, 3, 4). In this study, we didn't find any statistically significant correlation between UII and other parameters of the study like (GFR, blood urea serum creatinine and serum electrolytes), as the p value was> 0.05.

Table 2: Comparison of the mean±SE ofUII, GFR, blood urea and serum creatinine level before and after HD.

	Before	After
UII (Pg/ml)	103.8±7.42	100.7±9.29
GFR (ml/min)	20.34±4.46	40.27±8.23
Blood urea (mg/dl)	137.4±6.70	80.52±6.03
S. creatinine (mg/di)	6.27±0.36	3.77±0.30

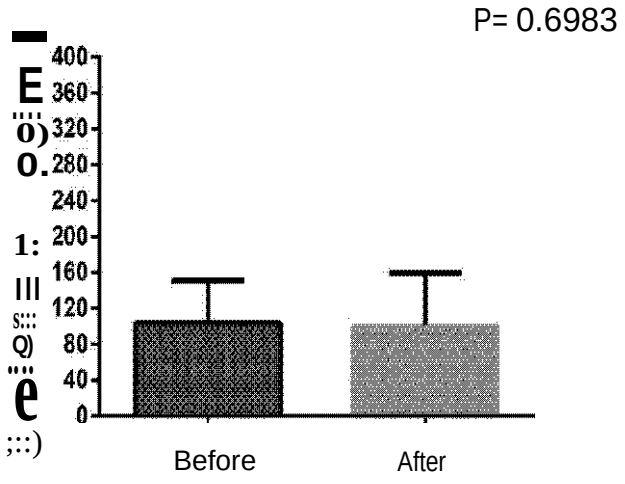

Figure 1: Plasma UII level before and after HD. The difference was not statistically significant as the P value is >0.05 (p =0.6983).

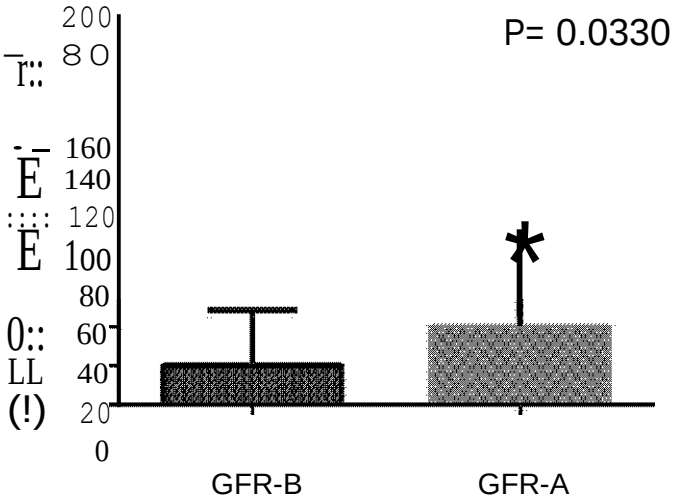

Figure 2: Level ofGFR before and after HD. The difference was statistically significant as the p value is <0.05 (p value= 0.0330).

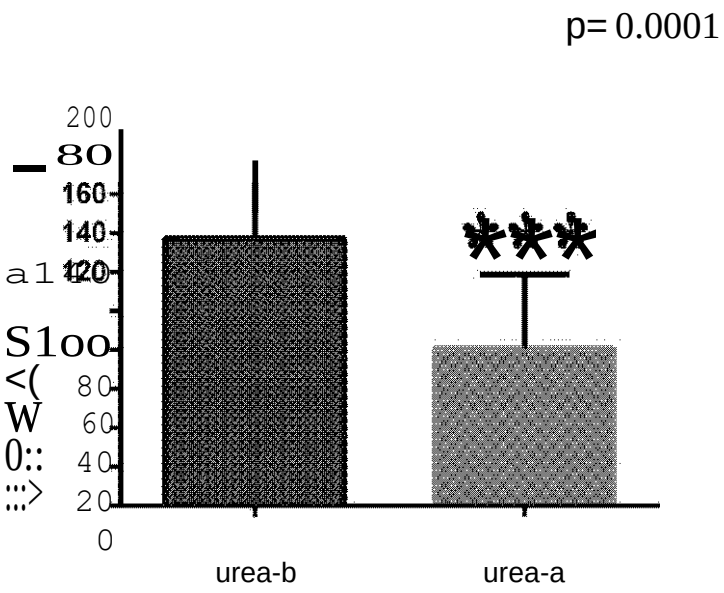

Figure 3: Showing the mean blood urea before and after HD.The difference was statistically highly significant as the P value is <0.05 (P value = <0.0001).

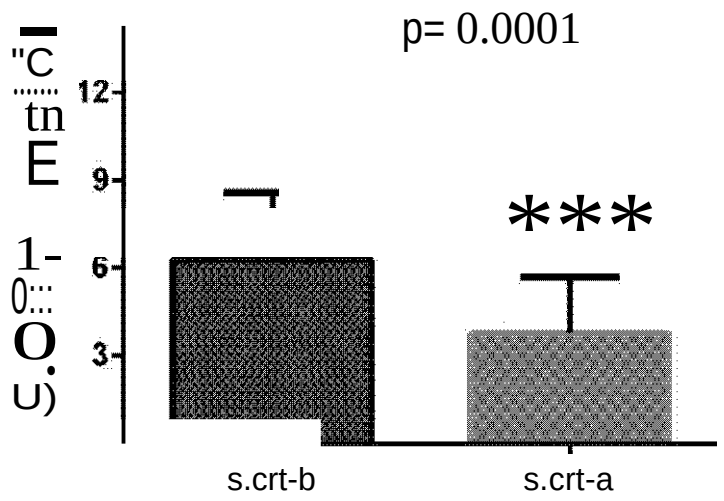

Figure 4: Showing the mean of creatinine level before and after HD. The difference was statistically highly significant as the p value is<0.05 (p value = <0.0001).

Discussion:

In this study we found that the HD has no significant effects on the level of UII. Although the mean of UII after HD has declined from (103.8-100.7pg/ml) but, it was statistically not significant as the p value is > 0.05 (p=0.6983), (Table 1 and Figure 1), in other related study like in Mosenki *et al*.[6] the mean UII has increased significantly after HD as the p value was <0.05 (p=0.008), The UII measurements in our study were made by enzyme-linked immunoassay, whereas the above study used radioimmunoassay. This difference in methodology may partly explain the difference in the results of these studies, another point could be due to the difference in patient populations between our study and the above one. Other studies like Totsune, *et al*.[7] and Mehmet Hursitoglu, *et al*.[8] they found different results in Totsune, *et al*.[7] the mean UII concentration was increased significantly after HD while in Mehmet Hursitoglu, *et al*.[8] the mean UII was increased, but the results were statistically not significant. We can only speculate that the insignificant effect of HD on the UII level in our study could be due to the following factors like, small sample size, the size of filter which is used in the dialysis machine, the duration of dialysis and the frequency of dialysis. For the future research it will be of great importance if the researcher could classify his subjects according to the above factors. In the present study the renal functions in the form of GFR, blood urea and serum creatinine were compared before and after HD, we found that the mean of GFR has increased significantly and this result is statistically significant as the p value is <0.05 (p=0.033), (Table 1 and Figure 2**).** We also found that the mean of blood urea and serum creatinine has declined significantly (Table 1 and Figure 3, 4). These results were statistically highly significant as the p value is <0.05. These results are consistent with the results of other related studies like in Mosenki *et al*.[6] and Noor ul Amin, *et al*.[9] , so we reached into a conclusion that HD has a statistically significant effect on renal functions, blood urea, serum creatinine.

Conclusion

The study concluded that the HD has no statistically significant effect on the level of UII before and after HD. The current study concluded that the HD has statistically significant effect on the level of GFR, blood urea and serum creatinine before and after HD. We concluded that there is no statistically significant correlation between UII and other parameters of the study like (GFR, blood urea and serum creatinine).

Conflicts of interest

The authors report no conflicts of interest.

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