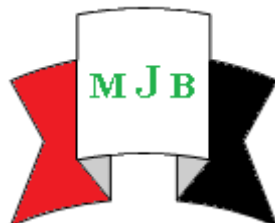


Physiological and Neurological Study of Chronic Renal Failure Patients with Continuous Hemodialysis

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Abstract

Chronic renal failure (CRF) has become a great problem throughout the world. It is connected to increased morbidity and mortality and also to decreased quality of life in patients compared to the general population. The study was designated to estimate some endocrinological disorder in CRF patients with continuous hemodialysis. Sixty patients (35 male & 25 female) were studied. Sixty healthy volunteers match in age and sex were enrolled and accepted as a control group, their range between (20-58 years). All patients and control underwent hormonal assessment for triiodothyronine hormone, thyroxine hormone, thyroid stimulating hormone, prolactin hormone, follicle stimulating hormone, luteinizing hormone, estradiol hormone and testosterone hormone by viadas technique, as well as biochemical assessment of blood urea, serum creatinine, total serum calcium and serum phosphorus. Assessment of cardiovascular autonomic neuropathy for male only with CRF. The study revealed that there was high frequency of hormonal disorder in CRF patients of both sex. Also the study revealed high frequency of cardiovascular autonomic neuropathy in CRF patients, therefore assessment of autonomic nervous system should be considered.

دراسة فسيولوجية وعصبية لمرض الفشل الكلوي المزمن مع الدليزة الدموية المستمر

الخلاصة

إن الفشل الكلوي أصبح مشكلة كبيرة في كافة أنحاء العالم، وله علاقة بزيادة المرضية والوفاء أيضا، ويؤدي إلى نقصان في نوعية الحياة بالمقارنة مع كافة السكان. الدراسة صممت لتقييم بعض وظائف الغدد في مرضى الفشل الكلوي المزمن مع الدليزة والذين خضعوا لتقييم سريري وكيميائي وحيوي. العدد الكلي للأشخاص الذين خضعوا للدراسة (١٢٠) شخصا منهم (٦٠) مريضا نحو (٦٠) سيطرة مجموعة السيطرة متوافقة مع المرضى من حيث العمر والجنس علما إن أعمار المرضى تتراوح بين (٢٠-٥٨) سنة. تم تقييم كامل للمرضى والمجموعة القياسية والذي تضمن تقييم سريري، تقييم النظام العصبي المستقل (للذكور فقط) ودراسة هرمونية لكل من الغدة الدرقية عن طريق فحص هرمون تروايودوثايرونين وفحص هرمون الثايروكسين وفحص الهرمون المحفز للغدة الدرقية بينما اختلال الوظائف التناسلية ثم تقييمه عن طريق هرمون الحلي، الهرمون المحفز للحوصلات المبيض والهرمون المحفز للجسم الأصفر وهرمون الاستروجين والهرمون الذكري. استنتجت الدراسة إن هناك نسبة عالية من اضطراب الهرمونات عند المصابين بالفشل الكلوي المزمن وكذلك الدراسة كشفت إن هناك نسبة عالية من اختلال عصبي مستقل عند المصابين بالفشل الكلوي المزمن لهذا فحص وتقييم الجهاز العصبي المستقل يجب أن يعتمد.

Introduction

Chronic kidney disease is considered a major global public health problem[20] and it can be defined as a reduced excretory kidney function ($GFR \leq 60 \text{ mL/min/1.73 m}^2$) or evidence of kidney damage for a period of at least 3 months [10,18]. End stage renal disease(Stage 5 Chronic Kidney disease) can be defined as a failure requiring dialysis or transplantation[5]. In patients with CRF different mechanisms lead to an alteration of endocrine responses include secretion of hormones and the function of their receptors may be altered by uremic toxicity which can promote an increased release of hormones such as parathyroid hormone [6]. The conversion of hormones into their active form may be disturbed as this could be demonstrated for the peripheral conversion of L-Thyroxin T4 to T3 [31]. Decreased renal production of hormones or essential regulators of hormones may occur in patients with chronic renal failure due to a reduction in functional renal mass [7].

Patients on HD due to CRF, there is a tendency towards a decrease (but generally still within the reference range) of T4 concentration, and low T3 and rT3 concentrations [3,22]. Sexual dysfunction and infertility are a common feature in CRF patients, and the occurrence of sexual dysfunction is about 50% to 70% in both male and female patients during dialysis and usually associated with pituitary-gonadal hormone disturbance, which does not reverse with renal replacement therapy [23]. The genesis of sexual dysfunction in male is multifactorial include hormonal disturbances, autonomic neuropathy, psychosocial factors, medications and Comorbid illness [8].

Materials and Methods

A cross sectional study of sixty patients with chronic renal failure with continuous hemodialysis at Artificial Kidney Unite in Marjan teaching hospital in Al-Hilla City. The study was conducted in the period from November 2012 to May 2013. sixty apparently healthy volunteer (35 male & 25 female) enrolled in the study, the patients and control groups are match in age and sex. the patients group consist of 35 male and 25 female. Their age range from 20-58 years, with a mean age of 43.72 ± 11.142 years. the control group consist of 35 male and 25 female with age range between 20-58 years, with a mean age of Patients group divided into three group according to duration of hemodialysis group1: duration of hemodialysis <18 months, group2: duration of hemodialysis 18-36 months and group3: duration of hemodialysis 36-54 months.

Hormonal study was done for patients and control group by viadas technique for prolactin hormone, follicle stimulating hormone, leutienizing hormone, estradiol hormone, testosterone hormone, T3, T4 and TSH as well as assessment of autonomic nervous system was done for male only by the fallowing test heart rate response to deep breathing, heart rate response to valsalva maneuver and heart rate response to standing (30/15 ratio) for parasympathetic system, while sympathetic system can be asses by blood pressure response to standing and blood pressure response to hand gripe.

Results

In this study number and percentage of chronic renal failure patients decrease as duration of hemodialysis increase. Regarding CRF female patients there was 14

patients (56%) who had history of menstrual cycle irregularity while only 5(20%) female of healthy subjects had history of menstrual cycle irregularity. Statistical analysis revealed high significant difference ($p<0.01$) between patients and control group and there was significant decrease ($p<0.05$) in testosterone hormone level and high significant increase ($p>0.05$) in estradiol hormone level in CRF female with menstrual cycle irregularity when compared with CRF female with regular menstrual cycle. Regarding CRF male patients there were 21 patients (60%) with history of erectile

dysfunction while in healthy control male 3 (9%) had history of erectile dysfunction as well as 19 patients (54.3%) were found to have cardiovascular autonomic neuropathy . Of these 3patients (15.8%) had early parasympathetic damage ,7 patients (36.8%) had definite parasympathetic and 9 patients (47.4%) had combined damage and there was high significant decrease ($p<0.01$) in testosterone hormone level in CRF male with erectile dysfunction in the other hand there is no significant increase ($p>0.05$) in estradiol hormone level in CRF male with erectile dysfunction.

Table 1 Mean value of prolactin hormone level in CRF and control group .

Hormone		Patients with CRF (duration of dialysis in months)			Healthy subjects
		<18 months (group1)	18- 36 months (group2)	36-54 months (group3)	Control (group4)
prolactin (ng/ml)	Male	40.13±28.64 (A)	37.44±22.34 (A)	50.07±14.5 (A)	12.3±5.1 (B)
	Female	55.83±30.34 (A)	45.62±20.72 (AB)	50.98±14.41 (C)	15.81± 6.8 (D)

Table 2 Mean values of Follicle stimulating hormone in CRF and control group

Hormone		Patients with CRF (duration of dialysis in months)			Healthy subjects
		<18 months (group1)	18-36 months (group2)	36-54 months (group3)	Control (group4)
FSH (mIU/ml)	Male	12.9 ± 2.13 (A)	14.26 ± 3 (A)	14.25 ± 5.19 (A)	4.6 ± 3.07 (B)
	Female	9.01 ± 4.6 (A)	9.82 ± 2.6 (A)	10.33 ± 4 (A)	5.51 ± 1.55 (B)

Table 3 Mean values of luteinizing hormone of CRF patients group and control group

Hormone		Patients with CRF (duration of dialysis in months)			Healthy subjects
		<18months (group1)	18- 36months (group2)	36-54 months (group3)	Control (group4)
LH mIU/ml	Male	13.37±4.13 (A)	15.68±3.4 (A)	15.6±3.31 (A)	4.62±2.89 (B)
	Female	13.68±2.42 (A)	12.86±3.14 (A)	12.66±2.56 (A)	5.67±4.75 (B)

Table 4 The values of estradiol hormone of CRF patients group and control group.

Hormone		Patients with CRF (duration of dialysis in months)			Healthy subjects
		<18 months (group1)	18- 36 months (group2)	36-54 months (group3)	Control (group4)
Estradiol (pg/ml)	Male	60.64±19.29 (A)	68.2±16.41 (A)	64.7±16.9 (A)	47.59±11.11 (B)
	Female	55.76±20.63 (A)	47.07±30.18 (A)	49.91±28.05 (A)	147.8±48.93 (B)

Table 5 Mean values of testosterone hormone of CRF patients and control groups.

Hormone		Patients with CRF (duration of dialysis in months)			Healthy subjects
		<18 months (group 1)	18- 36 months (group2)	36-54 months (group3)	Control (group4)
Testosterone (ng/dl)	Male	229.05±17.6 (A)	191.76±95.75 (A)	232.96±94.29 (A)	348.56±90.42 (B)
	Female	34.12±19.3 (a)	26.85±15.09 (a)	30.28±12.04 (a)	44.08±8.73 (b)

Table 6 Mean values of T3 and T4 hormone of CRF patients and control group.

Hormone		Patients with CRF (duration of dialysis in months)			Healthy subjects
		<18 months (group1)	18- 36 months (group2)	36-54 months (group3)	Control (group4)
T3 (nmol /L)	Male	1.05±0.18 (Aa)	0.87±0.27 (A)	0.67±0.12 (Ab)	1.54±0.36 (B)
	Female	1.02±0.15 (A)	0.72±0.3 (B)	0.76±0.16 (B)	1.42±0.19 (C)
T4 (nmol/L)	Male	85.65±15.13 (A)	87.66±15.74 (A)	88.2±7.83 (A)	83.87±8.86 (A)
	Female	83.56±11.87 (A)	91.05±37.52 (A)	88.08±11.33 (A)	87.62±4.57 (A)

Table 7 Mean values of TSH hormone of CRF patients and control group.

Hormone		Patients with CRF (duration of dialysis in months)			Healthy subjects
		<18 months (group1)	18-36 months (group2)	36-54months (group3)	Control (group4)
TSH (μmol/L)	Male	2.43±0.91 (Aa)	3.95±1.92 (Ba)	3.31±2.08 (Ab)	1.17±0.67 (C)
	Female	2.94±1.6 (AB)	3.55±1.85 (A)	4.43±1.1 (B)	1.97±0.27 (C)

-Values are mean ± SD.

-The values with different capital letter mean significant at 0.01 level.

The values with different small letters are significant at 0.05 level.

-The values with same letters are not significant at 0.05 level.

Discussion

The percentage of CRF patients to duration of dialysis is in agreement with other studies [27]. The explanation of this result is that dialysis patients are at a marked increased risk for premature death because of a high risk of cardiovascular and infectious complications[12]. In this study high percentage of CRF female patients presented with menstrual cycle irregularity when compared with control group. The same findings are reported by other studies [2,15].The explanation of this result that is

menstrual cycle irregularity associated with hypothalamic-pituitary gonadal dysfunction, as well as uremic coagulopathy and heparinization during HD intensify abnormal menstrual bleeding [24]. The results of this study show that high percentage of erectile dysfunction in CRF patients when compared with control group. This result is consistent with results of other studies [8,22]. The explanation of this result was that erectile dysfunction can occur due to decreased arterial blood flow, venous leakage due to shunts, altered penile smooth muscle function, hormonal disturbances, side

effect of medications, and neurogenic dysfunction[24]. It is revealed in this study that the percentage of CRF patients with CAN is 54.3%. This result match with results obtained by[19]. The explanation of this result that diabetes mellitus is a common cause of CRF and autonomic nervous dysfunction is a known complication of diabetes [28]. Another explanation is that CAN associated with hyperparathyroidism [16]. With regard to stage of CAN the result of this study revealed that parasympathetic dysfunction occurs with greater frequency than sympathetic dysfunction. This result agree with[16,17]. The explanation of this result impairment of vagal function has been found to be associated with diabetic nephropathy [28]. The result revealed that high significant increase in prolactin hormone level in CRF patients when compared with control groups. This result agree with result obtained from other studies [8]. The explanation of this result that an increase in serum prolactin levels is primarily due to decreased dopaminergic inhibition of prolactin release from pituitary gland and secondarily due to decreased LHRH release[24]. On the other hand, there is impairment of prolactin biodegradation by inefficient kidneys leads to hyperprolactinaemia [22]. There was a high significant increase in serum level of FSH hormone in CRF patients when compared with control group, also the study revealed that there is no significant decrease in level of FSH with continuous HD (between CRF patients groups). This result is consistent with other studies [26, 29]. The explanation of this result that increase level FSH hormone due to changes in hypothalamic-pituitary function the pulsatile secretion of GnRH is disturbed, (Gonadotrophin secretion is calcium dependent) so

disturbed calcium and phosphorous metabolism in CRF results in altered gonadotrophin secretion[24]. This study shows a significant increase in serum level of estradiol in male patients with CRF when compared with control group. These results were concurrent with [11]. The explanation of this result that decrease in pulsatile secretion of LH leads to elevating the serum estradiol and total estrogens level [24]. While in females, the result shows highly significant decrease in estradiol hormone level this result agrees with [1]. The explanation of this result that hyperprolactinemia contributes to ovarian dysfunction in women with continuous HD. The obtained results show high significant decrease in testosterone hormone level in CRF male patients and significant decrease in CRF female patients when compared with control group. This result agree with other studies [13,29]. The explanation of this result may be associated with significant decrease in pulsatile secretion of LH. This leads to low levels of testosterone in uremic patients. Another explanation is that low testosterone is due to decreased production, increased metabolic and dialytic clearance, alteration in testosterone binding capacity[21]. The study shows a statistically high significant decrease in T3 hormone. This is consistent with other studies done by [4,14]. The explanation of this result to reduction in T3 concentrations has been linked to a decrease in the peripheral conversion of T4 to T3 caused by an inhibition of 5' deiodinase levels chronic metabolic acidosis associated with the CKD may contribute in this effect. Another explanation that low T3 level could be due to clearance of free thyroid hormones through the dialysis membrane resulting in hypothyroidism [31]. In relation to thyroxin hormone the result of this

study revealed that there is no significant increase in thyroxin hormone level in CRF patients when compared with control group .This result agrees with studies obtained by[22,30].The explanation of this result that the ESRD may depend on the fact that the depression of T3 is much greater than that of T4, T3 being less tightly bound to thyroid-binding globulin than T4 [9]. The result of this study shows that there is a significant increase in TSH level in CRF patients when compared with control group. This result agrees with results got by[25] .The explanation of this result is that higher TSH levels in ESRD patients could be due to the effect of low circulating thyroid hormone levels on the pituitary by [14].

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