

## Renal function tests in hypertensive patients using atenolol

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### Abstract

Hypertension is strongly associated with functional and structural abnormalities that damage the kidneys, and other organs and lead to premature morbidity and death. This research is to study the renal function tests in hypertensive patients using Atenolol and comparing the results with that in newly diagnosed untreated hypertensive patient. In addition comparing these results with that of apparently normal residents living in Mosul as a control.

Eighty essential hypertensive patients were included in this study. They were divided into two groups, the first group included 50 patients (called Group A), with ages ranged from 38 - 65 years with a mean of  $49.86 \pm 7.02$  years, all were used Atenolol as antihypertensive mono therapy. The second group included 30 patients of newly diagnosed untreated hypertensive patients (called Group B), with ages ranged from 36-57 years with a mean of 44.9 years. A third group was the control group (called Group C), consisted of 30 normotensive subjects with ages ranged from 35-58 years with a mean of 45.9 years. The biochemical investigations carried were the renal function tests including serum; urea, creatinine, creatinine clearance, uric acid, sodium and potassium in addition to urine microalbuminuria.

A comparison between the means of serum urea in Group B with Group C showed a significant increase. In addition, there was a significant increase in serum uric acid in Group B in comparison with Group C. Moreover, MA level was significantly higher in Groups A and B when compared with Group C or when compared with each other. The dose of Atenolol showed a significant increase for MA with increased dose. The duration of treatment also showed a significant increase for MA with increased duration of treatment. In addition, age also causes a significant increase in MA with advanced ages and a decreased CreI in Group A.

The overall analysis of the renal function tests indicate that Atenolol although has a mild undesirable effects on renal functions but it has a negative effect on protein excretion, Moreover, untreated hypertensive patients showed more signs of undesirable effects of kidney function tests than treated patients with Atenolol specially in its effect on MA excretion.

**Keywords:** Serum, urea, creatinine, uric acid, microalbuminuria, sodium, potassium, hypertension, captopril.

### Introduction

Hypertension is the state of having high blood pressure (BP) (1). Progression of hypertension is strongly associated with functional and structural cardiac and

vascular abnormalities that damage the heart, kidneys, brain, vasculature, and other organs and lead to premature morbidity and death(2).

Hypertension is both a cause and an effect of renal impairment and its treatment influences renal outcomes (3).

Arteriosclerotic lesions of the afferent and efferent arterioles and the glomerular capillary tufts are the most common renal vascular lesions in hypertension and result in a decreased glomerular filtration rate and tubular dysfunction. Proteinuria and microscopic hematuria occurs because of glomerular lesions, and nearly 10% of death caused by hypertension result from renal failure (4).

Beta-adrenergic blockers have been widely used in the treatment of hypertension (5). Atenolol is a  $\beta_1$  selective blocker, it reduces the heart rate, which means it is useful in treating abnormally rapid heart rhythms and patients with high blood pressure (6).

The aims of the present study are to investigate the effects of Atenolol on renal function tests and to compare with untreated hypertensive patients and comparing these results with that of normal residents living in Mosul City as a control.

### **Patient and methods**

**Patients:** Eighty hypertensive patients of both sexes were included in this study, which was conducted during a period of 7 months from October 2008 till May 2009 with the co-operation of the medical staff of the out – patient's clinic in Ibn-Sina teaching hospital. The patients were divided into two groups. The first group (Group A) consisted of fifty patients whose blood pressure was controlled by using Atenolol (Monotherapy) in a dose ranged from 50 – 100 mg/day. The duration of treatment ranged from 2 months to 8 years and their ages ranged from 38 - 65 years with a mean of  $49.86 \pm 7.02$  years.

The second group (Group B) consisted of thirty patients who were newly diagnosed hypertensive patients with no treatment, and their ages ranged from 36 - 57 years with a mean of  $44.9 \pm 4.4$  years.

**Control (Group C):** Thirty apparently healthy individuals with ages ranged from

35 - 58 years with a mean of  $45.9 \pm 6.0$  years of both sexes were included in this study as a control group.

Patients or individuals with a history of heart, renal disease or diabetes mellitus or any other disease which may interfere with this study were excluded.

**Specimens and methods:** Venous blood were obtained from each individual of the three groups by antecubital venepuncture. Serum samples were used for the determination of urea, creatinine, creatinine clearance, sodium, potassium, and uric acid.

**Urine samples:** The first voided morning urine specimens were collected for determining the level of microalbuminuria.

All the biochemical analysis was performed at the laboratory of higher study in the department of Biochemistry, Mosul College of Medicine, University of Mosul, Mosul, Iraq. Serum levels of sodium and potassium was done at the laboratory of the kidney dialysis unit of Ibn-Sina teaching hospital.

Serum creatinine was measured by Jaffe reaction method (7) using a kit supplied by SYRBIO diagnostic reagents for laboratories under license of EURO BIO laboratories PARIS-France.

Creatinine clearance was measured by using the Cockcroft and Cault equation (8). Serum urea was measured by enzymatic method (9), using a kit supplied by Biomerieux (France).

Serum sodium and potassium were measured using FP20 flame photometer according to Burtis(10), using reagents supplied by SEAC-Italy.

Serum uric acid was measured by enzymatic method (11), using a kit supplied by BioLabo, France.

Urine microalbumin was measured by Micral test, according to Sacks and Bruns (12), using strips supplied by Roche Company, Germany.

**Statistical Analysis:**

The standard statistical methods used for the analysis of the data in this study were used to determine the mean and standard deviation (SD), to compare between cases with control, and to find the correlation between the various biochemical

parameters and the dose, duration of drugs used and age of the subjects (13).

### Results

The following tables show the results of all the present study.

### Discussion

In the present study the comparison between serum urea level in Group A and Group C and between Group A and Group B show no significant difference in serum urea (Table 1). This indicates that Atenolol has no adverse effect on kidney function in excreting urea. Whereas there was a significant increase in serum urea level in Group B in comparison with Group C ( $p < 0.05$ ) (Table 1).

This significant increase may be due to structural changes in the glomeruli of the kidneys in those patients, may be due to continued elevation of blood pressure, which leads to decrease GFR and finally increase in serum urea level (3).

This result is in agreement with the result of an other study (14), among the renal functions in patients with mild to moderate hypertension.

The comparison in this study between serum creatinine level in Group A and Group C showed no significant difference in serum creatinine level (Table 1), which means that Atenolol has no adverse effect on kidney functions in excreting creatinine. This result is in agreement with the result of another study in which they studied the effect of atenolol on renal hemodynamic in patients with uncomplicated essential hypertension. (15). The comparison between the level of serum creatinine in Group B and Group C and between Group A with Group B showed no significant difference, (Table 1). This is may be due to short duration of hypertensive effect on renal tissues or the disease is not sever enough to cause significant increase in serum creatinine level.

In this study, the comparison between Group A and Group C and between Group A with Group B, revealed no significant changes in serum creatinine clearance level (Table 1), this may indicate

that Atenolol has no adverse effect on creatinine clearance as a function of the kidneys .

These results are in agreement with another where they studied the effect Atenolol in patients with mild to moderate essential hypertension and they found that Atenolol produced a borderline decrease in renal plasma flow but no change in (GFR) or filtration fraction (16). Also no significant change in the level of creatinine clearance in Group B and Group C (Table 1). This result may be due to short duration of hypertensive effect on renal tissues or the disease is not sever enough to cause significant decrease.

In the present study the comparison between serum uric acid in Group A and Group C showed no significant changes, which is in agreement with another study (17), whereas the level of serum uric acid in Group B was significantly higher than serum uric acid level in Group C ( $p < 0.05$ ) (Table 1). It may be due to a decrease in renal blood flow which accompanies the hypertension which finally leads to increase uric acid reabsorption (18). This result is in agreement with the result of the study done by other investigators (19), where they found an association between serum uric acid and development of hypertension, and they suggested that uric acid was an independent predictor for the development and incidence of hypertension.

The comparison between Group A and Group C , Group A with Group B and Group B and Group C in microalbuminuria level showed a significant increase ( $p = 0.01$ ), ( $p < 0.01$ ) and ( $p < 0.001$ ) respectively (Table 2). These results indicate that Atenolol has a negative effect on urinary albumin excretion. The result of this study is in agreement with the result of another study (20). However the presence of microalbuminuria in patients with essential hypertension is a risk factor of cardiovascular morbidity and mortality (21).

In the present study the comparison between Group A and Group C showed no significant difference in serum level of sodium, also, no significant

difference in serum sodium level was found between Group A and Group B, between Group B and Group C (Table 1). This result indicates that Atenolol has no adverse effect in sodium excretion.

This result is in agreement with that of Hasan et. al., where they found no significant changes in serum level of sodium in their experimental study of Atenolol therapy (22).

In the present study the comparison between Group A and the Group C, Group A and Group B and Group B with Group C showed no significant difference in serum level of potassium (Table 1). These results indicate that Atenolol has no adverse effect in renal tubular function regarding potassium excretion.

The result of the present study is in agreement with the result obtained by other investigators (23).

The effect of dose and duration of Atenolol on renal function parameters in Group A in the present study had no significant effects. This result indicates that the effect of Atenolol is dose and duration independent. This result is in agreement with the result of another study, where they studied the effect of atenolol in doses of 50-100 mg daily on renal functions in hypertensive patients over a period of 3 years. They found no significant changes in renal function parameters (24). Whereas, the effect of the dose and duration of Atenolol on microalbuminuria in Group A and Group B was significantly higher than Group C ( $p < 0.01$ ) (Table 5 and 6 respectively).

This result may be due to the effect of hypertension on renal functions, which lead to increase protein excretion in the urine.

The effect of the age on the kidney function parameters in Group A in the present study was not significant except for creatinine clearance which was significantly lower than Group C ( $p = 0.01$ ) (Table 3) and this may be due to the decrease in GFR due to decreased renal blood flow with advancing age. Whereas, the effect of age in Group A, showed significant increase with advanced ages ( $p < 0.01$ ) (table 7).

### Conclusion

Atenolol although has a mild undesirable effects on renal functions but it has a negative effect on protein excretion, so it is not preferable for the management of hypertensive patients with microalbuminuria.

Moreover, untreated hypertensive patients shows more signs of undesirable effects of kidney function tests than treated patients with of Atenolol specially in its effect on microalbuminuria excretion.

It is advisable that hypertensive patients with microalbuminuria to have periodic check of renal function parameters because it is an early sign for renal tissues damage.

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Table (1): Comparison of kidney function parameters between all the three groups (Group A, Group B, and group C)

Parameters	Mean $\pm$ SD			T-test	p-value
	Control group (C) (n=30)	Atenolol group (A)(n=50)	Newly diagnosed (B)(n=30)		
Sodium (mmol/L)	138.97 $\pm$ 1.92	138.56 $\pm$ 2.56	139.97 $\pm$ 4.02	A/C A/B B/C	0.454 0.224 0.059
Potassium (mmol/L)	4.04 $\pm$ 0.29	4.22 $\pm$ 0.48	4.16 $\pm$ 0.44	A/C A/B B/C	0.069 0.215 0.576
Urea (mg/dL)	30.08 $\pm$ 4.3	31.23 $\pm$ 5.36	32.75 $\pm$ 4.75	A/C A/B B/C	0.322 0.039 0.254
Creatinine (mg/dL)	0.78 $\pm$ 0.14	0.77 $\pm$ 0.14	0.80 $\pm$ 0.20	A/C A/B B/C	0.767 0.660 0.445
Uric acid (mg/dL)	5.14 $\pm$ 0.92	5.34 $\pm$ 0.90	5.67 $\pm$ 0.81	A/C A/B B/C	0.346 0.020 0.100
Crcl (ml/min)	90.07 $\pm$ 16.71	83.01 $\pm$ 16.17	88.21 $\pm$ 16.61	A/C A/B B/C	0.075 0.675 0.172

NS = Not significant using unpaired t-test

**Table (2):** Microalbumin (MA) levels in the studied groups.

Groups MA	Atenolol		Control		Newly diagnosed	
	No.	%	No.	%	No.	%
1. MA <20mg/l(-ve)	7	14.0	0	0.0	1	3.3
2. MA ca.20mg/l	2	4.0	0	0.0	3	10.0
3. MA ca.50mg/l	6	12.0	0	0.0	8	26.7
4. MA ca.100mg/l	35	70.0	30	100	18	60.0
Total	50	100	30	100	30	100

Group A x Group C (p = 0.011), Group A x Group B (p=0.0017),  
Group B x Group C (p<0.001) according to Fisher Freeman Halton test.

**Table (3):** Effect of age on kidney function parameters in *Group A*

Age (year) Parameters	Mean ± SD		p-value
	40-50 (n=26)	51-60 (n=24)	
Sodium (mmol/L)	139.0 ± 2.47	138.08 ± 2.62	0.209 (NS)
Potassium (mmol/L)	4.20 ± 0.54	4.25 ± 0.41	0.762 (NS)
Urea (mg/dL)	31.51 ± 5.32	30.93 ± 5.5	0.705 (NS)
Creatinine (mg/dL)	0.77 ± 0.16	0.76 ± 0.12	0.730 (NS)
Uric acid (mg/dL)	5.19 ± 0.93	5.49 ± 0.86	0.246 (NS)
Crcl (ml/min)	88.52 ± 12.64	77.04 ± 17.66	0.011

NS = Not significant using unpaired t-test.

**Table (4):** Effect of age on kidney function parameters in *Group B*

Parameters	Age		p-value
	(year)	Mean ± SD	
	40-50 (n=27)	51-60 (n=3)	
Sodium (mmol/L)	139.96 ± 4.21	140.00 ± 2.0	0.988 (NS)
Potassium (mmol/L)	4.15 ± 0.46	4.27 ± 0.31	0.677 (NS)
Urea (mg/dL)	32.18 ± 4.52	38.5 ± 3.54	0.071 (NS)
Creatinine (mg/dL)	0.77 ± 0.14	1.03 ± 0.47	0.025
Uric acid (mg/dL)	5.69 ± 0.83	5.50 ± 0.72	0.708 (NS)
Crcl (ml/min)	88.65 ± 16.58	84.23 ± 20.08	0.670 (NS)

NS = Not significant using unpaired t-test

**Table (5):** Effect of Atenolol dose on MA levels.

Atenolol dose MA	50 (mg/day)		100 (mg/day)		p-value
	No.	%	No.	%	
1	1	5.6	6	18.8	0.009
2	0	0.0	2	6.3	
3	4	22.2	2	6.3	
4	13	72.2	22	68.8	
Total	18	100	32	100	

Using Fisher Freeman Halton test.

Table (6): Effect of duration of treatment on MA levels in *Group A*

Duration	MA	<1(yr)		>1-2.5(yr)		2.5-5(yr)		p-value
		No.	%	No.	%	No.	%	
Atenolol	1	2	15.4	2	13.3	3	13.7	0.0023
	2	0	0.0	1	6.7	1	4.5	
	3	3	23.1	1	6.7	2	9.1	
	4	8	61.5	11	73.3	16	72.7	

Using Fisher Freeman Halton test

Table (7): Effect of age on MA levels in all studied groups

Groups	MA	40-50		51-60		p-value
		No.	%	No.	%	
<i>Group A</i>	1	2	7.7	5	20.8	0.003
	2	1	3.8	1	4.2	
	3	1	3.8	5	20.8	
	4	22	84.6	13	54.2	
<i>Group C</i>	1	0	0.0	1	6.7	NS
	2	0	0.0	0	0.0	
	3	0	0.0	0	0.0	
	4	23	100	7	100	
<i>Group B</i>	1	1	3.7	0	0.0	0.124(NS)
	2	3	11.1	0	0.0	
	3	6	22.2	2	66.7	
	4	17	63.0	1	33.3	

NS = Not significant according to Fisher Freeman Halton test.

## فحوصات وظائف الكلية لدى المرضى المصابين بفرط ضغط الدم من الذين يتناولون دواء الأتينولول

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الخلاصة

لقد وجدت علاقة واضحة بين ارتفاع ضغط الدم وبين التغيرات الوظيفية والتركيبية للكلى وغيرها من الأعضاء مما يؤدي إلى الموت المبكر. وقد اجري هذا البحث لدراسة تأثير عقار الأتينولول على فحوصات وظائف الكلية لدى المرضى المصابين بفرط ضغط الدم، ومقارنة هذه النتائج مع تلك النتائج المأخوذة من المرضى المشخص لديهم حديثا فرط ضغط الدم ممن لم يتناولوا بعد أي علاج لفرط ضغط الدم. ثم مقارنة نتائج هاتين المجموعتين مع مجموعة أشخاص أصحاء ظاهريا من الساكنين في مدينة الموصل كمجموعة ضابطة.

أجريت هذه الدراسة على ثمانين مريضا مصابين بفرط ضغط الدم الأساسي. وقد تم تقسيم المرضى إلى مجموعتين. شملت المجموعة الأولى خمسين مريضا (أطلق عليها مجموعة أ) 49.86 سنة وجميعهم يتناولون عقار 7.02  $\pm$  تتراوح أعمارهم من 38-65 سنة وبمعدل الأتينولول كعلاج لفرط ضغط الدم. أما المجموعة الثانية فشملت 30 مريضا بفرط ضغط الدم شُخص حديثا ولم يستعملوا بعد أي علاج لفرط ضغط الدم (أطلق عليها مجموعة ب) وتتراوح أعمارهم من 36-57 سنة وبمعدل 44.9 سنة. أما المجموعة الثالثة وهي مجموعة الضبط (أطلق عليها مجموعة ج) فتتكون من 30 شخص بأعمار تتراوح بين 35-58 سنة وبمعدل 45.9 سنة. وقد شملت فحوصات وظائف الكلية قياس تركيز كل من اليوريا، الكرياتينين، تصفية الكرياتينين، حامض البوليك، الصوديوم، البوتاسيوم في مصل الدم وقياس معدل الزلال البولي الدقيق.

أظهرت نتائج هذا البحث زيادة معنوية في معدل مستوى اليوريا في مصل الدم عند المجموعة ب عند مقارنتها مع المجموعة ج. إضافة إلى ذلك فقد وجدت زيادة معنوية في مستوى حامض البوليك في مصل الدم المأخوذة من المجموعة ب مقارنة بالمجموعة ج. إلى جانب ارتفاع معنوي في مستوى معدل الزلال البولي الدقيق في المجموعتين أ و ب مقارنة بالمجموعة ج، أو عند مقارنتهم ببعضهم. كما ارتبط تأثير كل من زيادة جرعة الأتينولول وزيادة مدة العلاج وتقدم العمر بزيادة معنوية في مستوى معدل الزلال البولي الدقيق. كذلك اتضح أن تقدم العمر أدى إلى نقصان معنوي في تصفية الكرياتينين لدى المجموعة أ.

إن التحليل الإحصائي الكلي لهذه الدراسة على فحوصات وظائف الكلية يوضح أن عقار الأتينولول رغم انه لا يتسبب إلا بتأثيرات سلبية قليلة على وظائف الكلية. كما تبين من هذه الدراسة وجود ملاحظات للتأثيرات السلبية على وظائف الكلية لدى المرضى المصابين بفرط ضغط الدم ممن لا يتناولون أي عقار لعلاج فرط ضغط الدم خاصة في معدل الزلال البولي الدقيق.