STUDY OF RENAL FUNCTION AFTER THROMBOLYTIC THERAPY IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

Thrombolytic therapy, the important therapeutic agents in patients with acute myocardial infarction has been reported to be associated with significant early onset proteinuria.

The aim of this study was to determine whether streptokinase therapy is associated with changes in renal function (both glomerular and tubular) in excess of that expected in an acute vascular event; and the possible pathogenesis of any observed changes among patients with uncomplicated acute myocardial infarction.

Our work comprised 30 patients with uncomplicated acute myocardial infarction selected from coronary care unit Mansoura Emergency Hospital.

They comprised 15 patients who received streptokinase therapy (thrombolytic group) and 15 patients who did not receive streptokinase therapy (non thrombolytic group).

Laboratory tests reflecting both glomerular functions (serum creatinine, creatinine clearance and urinary albumin excretion) and tubular functions (serum and urinary B₂ microglobulin) were estimated for every patient on admission; 24 hours after initiation of therapy as well as on the 7th day of therapy.

The results showed:

A) Non significant changes in renal functions among patients with acute myocardial infarction not receiving thrombolytic therapy.

B) Thrombolytic therapy induced:

(1) Non significant changes in serum creatinine, creatinine clearance and serum B2 microglobulin; (2) transient glomerular impairment in the form of only increase in urinary albumin excretion and microalbuminuria that occurred 24 hr after therapy and disappeared by the 7th day and (3) mild renal tubular impairment in the form of significant increase in urinary B2 microglobulin excretion that occurred 24 hr after therapy and persisted on the 7th day.

The abnormal excretion of urinary albumin and B2-microglobulin were related to effective thrombolytic therapy and improved left ventricular performance.

The changes in the laboratory parameters after thrombolytic therapy were unrelated to presence or absence of associated diabetes mellitus, hypertension; mild renal impairment and dyslipidemia.

Conclusion :

Thrombolytic therapy can be used safely (unless there is other contraindication) among patients with diabetes mellitus, hypertension, dyslipidemia as well as with mild renal impairment.

INTRODUCTION

Acute myocardial infarction is a serious medical emergency resulting in most cases from complete thrombotic occlusion of infarct-related coronary artery causing myocyte necrosis (1). Occlusion of a coronary artery leading to acute myocardial infarction appears to be the final common pathway resulting from a complex and dynamic interaction of coronary atherosclerosis, vasospasm and platelet activation ultimately leading to coronary artery thrombosis (2,3,4).

In the presence of uncomplicated acute myocardial infarction, patients may show renal vasodilatation, and the elevation of atrial natriuretic peptides may play some role in this process(5). Both pre-renal azotemia and acute renal failure can complicate the marked reduction of cardiac output that occurs in cardiogenic shock(6). A physiologic compensation for this can occur by the increase in atrial natriuretic peptide, following acute myocardial infarction. The later increase is correlated with the degree of left ventricular failure (5).

Thrombolytic therapy is a traditional measure in treatment of acute myocardial infarction, which is believed to

re-establish coronary blood flow (7). Streptokinase is a foreign protein and disadvantage to treatment with it is the occasional occurrence of immune reaction (8). Proteinuria may be a subclinical response that could be related to circulating specific antibody present at time of treatment (9).

Streptokinase was associated with significant early onset proteinuria of glomerular origin. This started to resolve by day 3 and without deterioration in overall renal function. The temporal relation to the initial fall in antibody titer suggests that it could be the result of immune complex deposition in the glomeruli (10).

The aim of this study was : (1) to determine wheather streptokinase therapy is associated with changes in renal function (both glomerular and tubular) in excess of that expected in an acute vascular event; (2) to determine the possible nature and etiology of any observed change and (3) the possible relation of any renal change to the presence of other concomitant diseases among patients with uncomplicated acute myocardial infarction.

PATIENTS AND METHODS

The present study comprised 30

patients with uncomplicated acute myocardial infarction who were admitted and managed at coronary care unit Mansoura Emergency Hospital. They were 25 males and 5 females with ages ranging from 40 to 70 years (57.5 ± 8.7).

Patients were classified into two groups according to use of thrombolytic therapy:-

(A) Group receiving streptokinase which comprised 15 patients (the thrombolytic group).

(B) Group not receiving streptokinase (the non-thrombolytic group) which comprised 15 patients (and received only conventional therapy). Streptokinase was not given because of presence of any contraindication for its use.

Diagnosis of acute myocardial infarction was based on 2 of 3 criteria: (1) typical chest pain (2) definite electrocardiographic changes (ST elevation of at least 1 mm in 2 limb leads or 2 mm in 2 adjacent chest leads) and (3) rise in serum creatine phosphokinase (CPK) enzyme activity (11).

Based on clinical, electrocardiographic, echocardiographic and laboratory data, we excluded from our

study patients with : previous myocardial infarction, cardiogenic shock, congestive heart failure, collagen diseases, systemic vasculitis, urinary tract infection (pus cells > 5/HPF), patients with initial microalbuminuria on admission, as well as patients with chronic renal disease or failure (creatinine clearance < 30 ml/min).

All patients were subjected to the following :

A- Thorough clinical evaluation and continuous monitoring and serial ECG recording.

B- Laboratory Investigations :-

1) Cardiac enzymes:

- Creatinine phosphokinase (CPK) (on admission and after 24 & 36 hours) :
- Total CPK: By a three-step coupled enzyme system (12).
- CPK-MB isoenzyme: By immunoassay method (13).
- Lactic dehydrogenase (LDH) (on admission and after 24 & 48 hours): By the biodynamic calorimetric procedure (14).

2) Some laboratory tests reflecting renal functions (three samples were taken: on admission, 24hr and 7 days after admission).

a) Test reflecting glomerular function.

- Serum creatinine, urinary creatinine and estimation of creatinine clearance: By alkaline picric acid method (15).
- Urine albumin level (16).

b) Test reflecting tubular function.

- Urine B2 microglobulin level: Enzymatic immunoassay (17).
- Serum B2 microglobulin level: Enzymatic immunoassay (17).

3) Complete urine analysis, and determination of total urinary protein (18).

4) Some liver function tests:

- Serum albumin: Calorimetric determination (19).
- Serum bilirubin (20).
- Amino transferases (ALT & AST): By Calorimetric method (Transaminase kits) (21).

5) Complete blood picture.

6) Erythrocyte sedimentation rate (ESR).

7) Lipogram includes:

- Serum cholesterol: Enzymatic determination (22)
- Serum triglyceride: Enzymatic determination (23).
- HDL cholesterol and LDL cholesterol (24).

8) Fasting & 2hr post-prandial

blood sugar.

C- Plain x-ray chest PA view for, cardiomegaly, signs of lung congestion (25).

D- Echocardiographic examination (5-7 days after admission) for:

a) M-mode assessment of left ventricular dimensions and function via detection of end-systolic diameter, end-diastolic diameter, ejection fraction (EF), percent fractional shortening. (26)

b) Two dimensional analysis of segmental wall motions. (26)

E- Abdominal ultrasound.

The thrombolytic group was subdivided according to clinical and laboratory parameters as follows:

- 1- Presence of hypertension (9 patients hypertensive and 6 patients normotensive).
- 2- Presence of diabetes mellitus (7 patients diabetics and 8 patients not diabetics).
- 3- Creatinine clearance (6 patients with creatinine clearance > 80ml/min and 9 patients with creatinine clearance < 80ml/min).
- 4- Serum cholesterol level (8 patients with cholesterol level >

200mg/dl and 7 patients with cholesterol level $\leq$ 200mg/dl).

RESULTS

1) The studied thrombolytic and non thrombolytic groups were well matched as regard age, blood pressure, blood glucose level, presence of hypertension, diabetes mellitus and site of infarction (table 1) and initial laboratory parameter (table 2).

2) Thrombolytic group showed significant increase in EF and %FS than the non thrombolytic group reflecting better left ventricular performance (table 1).

3) The non thrombolytic group showed non significant serial changes in any test reflecting renal functions (table 3 & Figur 1,2).

4) The whole thrombolytic group (tables 4 & 5 & Figure 1,3) and the different thrombolytic subgroups (tables 6-9) showed:-

- Absence of clinical proteinuria.
- Significantly increased urinary albumin excretion and increased incidence of microalbuminuria 24 hr after thrombolytic therapy that returned to normal by the 7th day of therapy ($P < 0.05$).
- Significantly increased excretion of urinary B2-microalbumin and increased incidence of abnormal B2-uri-

nary microglobulin level 24 hr after thrombolytic therapy that persisted up to 7th day of therapy ($P < 0.05$).

- Non significant serial changes in serum creatinine; creatinine clearance and serum B2-microglobulin.

5) Non significant changes in all serial renal laboratory tests on comparing various thrombolytic sub-groups:-

- Diabetics and non-diabetics (table 6).

- Hypertensives and non-hypertensives (table 7).

- Mild renal impairment and normal renal function (table 8).

- Dyslipidemics and non-dyslipidemics (table 9).

6) Significant positive correlation between: (1) left ventricular (LV) ejection fraction and urinary albumin level ($r = +0.540$; $P < 0.05$) and (2) LV percent fibre shortening and urinary albumin level ($r = +0.637$; $P < 0.05$) (table 10).

7) Significant negative correlation between: (1) CPK and urinary B2 microglobulin ($r = -0.565$; $P < 0.05$); (2) LDH and urinary albumin ($r = -0.509$; $P < 0.05$) and (3) LDH and urinary B2 microglobulin ($r = -0.565$; $P < 0.05$) (table 10).

Figure (1) : Urinary albumin excretion rate ($\mu\text{g/day}$) among non-thrombolytic and thrombolytic groups.

Figure (2) : Urinary B2-microglobulin excretion rate among the non-thrombolytic and thrombolytic groups.

Figure (3) : Serial incidence of microalbuminuria and abnormal B2-microglobulin among the thrombolytic group.

Table (1): Comparative analysis of some clinical and echocardiographic parameters in thrombolytic versus non thrombolytic group.

Parameters	Thrombolytic group (n = 15)		Non thrombolytic group (n = 15)		P value
Age (years)	58.0	± 8.8	57.0	± 9.3	>0.05
Systolic BP (mmHg)	128	± 24	108	± 29	>0.05
Diastolic BP (mmHg)	81	± 15	75	± 13	>0.05
Fasting BL glucose (mg/dl)	193	± 24	181	± 52	>0.05
2 hr PP BL glucose (mg/dl)	203	± 65	195	± 70	>0.05
Hypertension (no)	9	60%	6	40%	>0.05
Diabetes mellitus (no)	7	46.67%	5	20.0%	>0.05
Anterior MI (no)	10	66.67%	7	46.67%	>0.05
Inferior MI (no)	5	30.3%	8	53.53%	>0.05
LV-ESD (MV ± SD)	3.82	± 0.32	3.98	± 0.43	>0.05
LV-EDD (MV ± SD)	5.66	± 0.62	5.34	± 0.51	>0.05
EF (MV ± SD)	64	± 10.8	55	± 13	<0.05
%FS (MV ± SD)	33.6	± 8.1	26.4	± 10.4	<0.05

LV-ESD = Left ventricle systolic dimension.

LV-EDD = Left ventricle diastolic dimension.

MI = Myocardial infarction.

%FS = Percent fractional shortening.

BP = Blood pressure.

EF = Ejection fraction.

BL = Blood.

Table (2): Comparative analysis of some laboratory parameters in thrombolytic versus non thrombolytic group (admission values).

Parameters	Thrombolytic group (n = 15)		Non Thrombo. group (n = 15)		P value
Lipogram (gm/dl):					
HDL . cholesterol	43.0	±13.0	41.0	±11.0	>0.05
LDL . cholesterol	150	±39	153	±38	>0.05
Total cholesterol	214	±40	207	±45	>0.05
Triglyceride	125	±60	117	±60	>0.05
ESR:					
1 st hour	19	±11	22.7	±15	>0.05
2 nd hour	33	±18	43	±24	>0.05
Liver functions:					
Albumin (gm/l)	4.1	±0.2	3.9	±0.3	>0.05
ALT (u/ml)	45	±52	36	±39	>0.05
AST (u/ml)	63	±60	50	±26	>0.05
Bilirubin (mg/dl)	0.9	±60	0.8	±0.4	>0.05
CPK (u/ml)	462	±520	560	±633	>0.05
LDH (u/ml)	360	±156	318	±191	>0.05
Serum creatinine (mg/dl)	1.2	±0.5	1.1	±0.4	>0.05
Creatinine clearance (ml/min)	105.2	±23.3	108.6	±16.3	>0.05
Urinary albumin (µg/ml)	4.7	±2.96	4.7	±2.1	>0.05
Urinary B₂-micro-globulin (µg/24h)	105.3	±103.8	150.9	±150.7	>0.05
Serum B₂-micro-globulin (µg/dl)	106.9	±16.4	105.4	±15.3	>0.05

ESR = Erythrocyte sedimentation rate.

CPK = Creatinine phosphokinase.

LDH = Lactic dehydrogenase.

Table (3): Comparative analysis of serial changes in some laborator tests reflecting renal function among the non-thrombolytic group (group not receiving streptokinase).

Parameter	Admission value	Day 1 value	Day 7 value	Signif.
S.Creatinine (mg/dl)	1.130 ±0.40	0.90 ±0.50	0.9 ±0.4	P>0.05
Creatinine clearance (ml/min)	108.6 ±16.3	100.2 ±15.2	103.1 ±17.6	P>0.05
Urinary albumin excretion (µg/dl)	4.7 ±2.1	3.5 ±2.7	4.6 ±3.5	P>0.05
Urinary B2-microglobulin (µg/24hr)	150.9 ±150.7	137.0 ±199.7	140.6 ±121.0	P>0.05
Serum B2-microglobulin (µg/dl)	105.4 ±15.3	104.2 ±17.6	107.4 ±14.3	P>0.05
Incidence of proteinuria (>150mg/day)	0 Zero%	0 Zero%	0 Zero%	P>0.05
Incidence of micro-albuminuria (>20µg/ml)	0 Zero%	0 Zero%	0 Zero%	P>0.05
Incidence of urinary B2-micro-globulin (>370µg/24hr)	0 Zero%	0 Zero%	0 Zero%	P>0.05

Table (4): Comparative analysis of serial changes in some parameters reflecting renal function among the thrombolytic group (SK-subgroup).

Parameter	Admission valve	Day 1 valve	Day 7 valve	Signif. (F-test)
S.Creatinine (mg/dl)	1.2 ±0.5	1.3 ±0.9	1.2 ±0.8	P>0.05
Creatinine clearance (ml/min)	105.2 ±23.3	83.6 ±17.4	91.7 ±18.6	P>0.05
Urinary albumin excretion (µg/dl)	4.7 ±2.96	53.6 ±26.6	8.8 ±4.2	P<0.05
Urinary B2- microglobulin excretion (µg/24hr)	105.3 ±103.8	333.2 ±405.6	370.2 ±330.6	P<0.05
Serum B2- microglobulin (mg/dl)	106.9 ±16.4	104.9 ±20.4	108.4 ±14.5	P>0.05
Incidence of proteinuria (>150mg/day)	0 Zero%	0 Zero%	0 Zero%	P>0.05
Incidence of micro- albuminuria (>20µg/ml)	0 Zero%	12 80%	0 Zero%	P<0.05
Incidence of urinary B2-micro-globulin (>370µg/24hr)	0 Zero%	5 32.33%	7 44.66 %	P<0.05

Table (5): Comparative analysis of incidence of mircoalbuminuria (> 20 ug/min) and abnormal urinary B2-microglobulin excretion (> 370 ug/day) among non thrombolytic and different thrombolytic subgroups.

Studied group	Microalbuminuria			Abnormal urinary B2 microglobulin			
	Adm. n %	Day 1 n %	Day 7 n %	Adm. n %	Day 1 n %	Day 7 n %	
Non thrombolytic group (15)	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	
Total thrombolytic gp (15)	0 0%	12 80%	0 0%	0 0%	5 33.3%	7 44.6%	
Diabetic (7)	0 0%	6 85.7%	0 0%	0 0%	2 28.6%	3 42.9%	
Non-diabetic (8)	0 0%	6 87.5%	0 0%	0 0%	3 37.5%	4 50%	
	P> 0.05	P> 0.05	P> 0.05	P> 0.05	P> 0.05	P> 0.05	
Hypertensive (9)	0 0%	8 88.8%	0 0%	0 0%	3 33.3%	5 44.44%	
Non-hypertens. (6)	0 0%	4 66.6%	0 0%	0 0%	2 33.3%	2 33.33%	
	P> 0.05	P> 0.05	P> 0.05	P> 0.05	P> 0.05	P> 0.05	
Abnormal creat. (6)	0 0%	5 83.3%	0 0%	0 0%	2 33.33%	3 50.0%	
Normal creat. (9)	0 0%	7 77.77%	0 0%	0 0%	3 3.33%	4 44.44%	
	P> 0.05	P> 0.05	P> 0.05	P> 0.05	P> 0.05	P> 0.05	
Dyslipidemic (8)	0 0%	7 78%	0 0%	0 0%	3 7.5%	4 50.0%	
Normal lipid (7)	0 0%	5 83%	0 0%	0 0%	2 28.75%	3 42.9%	
	P> 0.05	P> 0.05	P> 0.05	P> 0.05	P> 0.05	P> 0.05	

Group number in between practice.

Table (6): Comparative analysis of serial changes in some renal function test among the thrombolytic group (Diabetic versus non diabetic subgroups).

Laboratory parameter	Admission valve		First day valve		Day 7 valve		Significance (F-test)
	MV	SD	MV	SD	MV	SD	
S.creatinine							
Diabetic gp	1.50	±0.616	1.56	±0.960	1.60	±0.698	P > 0.05
Non-diabetic gp	1.09	±0.24	1.15	±0.611	1.09	±0.748	P > 0.05
	P > 0.05		P > 0.05		P > 0.05		
Cr. clearance							
Diabetic gp	96.30	±17.80	78.7	±13.8	84.70	±21.17	P > 0.05
Non-diabetic gp	112.8	±23.20	86.5	±18.8	97.07	±14.30	P > 0.05
	P > 0.05		P > 0.05		P > 0.05		
Serum B₂ microglob.							
Diabetic gp	109.0	±16.2	108.0	±18.3	108.6	±14.7	P > 0.05
Non-diabetic gp	108.0	±15.0	107.0	±16.8	106.0	±15.0	P > 0.05
	P > 0.05		P > 0.05		P > 0.05		
Urinary albumin							
Diabetic gp	5.02	±2.40	62.60	±20.30	9.03	±3.60	P < 0.05
Non-diabetic gp	4.40	±3.50	46.80	±28.40	6.65	±2.30	P < 0.05
	P > 0.05		P > 0.05		P > 0.05		
Urinary B₂ microglobulin							
Diabetic gp	98.60	±120.6	226.1	±294.2	390	±366.0	P < 0.05
Non-diabetic gp	112.2	±99.8	376.2	±393.4	318	±209.8	P < 0.05
	P > 0.05		P > 0.05				

Diabetic group comprised 7 patients.

Non-diabetic group comprised 8 patients.

Table (7): Comparative analysis of serial changes in some renal function test among the thrombolytic group (Hypertensive versus non hypertensive subgroups).

Laboratory parameter	Admission valve	First day valve		Day 7 valve		Significance (F-test)
	MV SD	MV	SD	MV	SD	
S.creatinine						
Hypertensive gp	1.44 ±0.753	1.5	±0.986	1.39	±0.680	P > 0.05
Non-hypertensive gp	0.95 ±0.607 P > 0.05	1.10	±0.420 P > 0.05	0.95	±0.63	P > 0.05
Cr. clearance						
Hypertensive gp	101.22 ±24.36	79.84	±17.24	85.11	±20.40	P > 0.05
Non-hypertensive gp	110.67 ±20.14 P > 0.05	90.35	±15.05 P > 0.05	95.60	±18.12 P > 0.05	P > 0.05
Serum B₂ microglob.						
Hypertensive gp	98.67 ±25.49	103.89	±18.67	115.36	±11.75	P > 0.05
Non-hypertensive gp	106.5 ±22.06 P > 0.05	106.5	±16.29 P > 0.05	104.0	±16.79 P > 0.05	P > 0.05
Urinary albumin						
Hypertensive gp	4.49 ±2.48	62.22	±19.01	9.02	±4.29	P < 0.05
Non-hypertensive gp	4.06 ±3.82 P > 0.05	40.67	±20.47 P > 0.05	8.50	±4.46 P > 0.05	P < 0.05
Urinary B₂ microglobulin						
Hypertensive gp	110.33 ±109.8	296.44	±235.43	329.0	±343.2	P < 0.05
Non-hypertensive gp	101.50 ±94.2 P > 0.05	38.40	±418.0 P > 0.05	485.0	±371.0 P > 0.05	P < 0.05

Hypertensive group comprised 9 patients.

Non-hypertensive group comprised 6 patients.

Table (8): Comparative analysis of serial changes in some renal function test among the thrombolytic group (mild renal impairment versus normal renal subgroups).

Laboratory parameter	Admission valve		First day valve		Day 7 valve		Significance (F-test)
	MV	SD	MV	SD	MV	SD	
S.creatinine							
Mild renal impairment gp	1.62	±0.509	2.03	±0.98	1.48	±0.568	P > 0.05
Normal renal gp	0.944	±0.150	1.024	±0.402	1.04	±0.398	P > 0.05
	P < 0.05		P < 0.05		P < 0.05		
Cr. clearance							
Mild renal impairment gp	72.83	27.80	60.3	±21.9	68.7	±17.2	P > 0.05
Normal renal gp	119.7	18.58	93.7	±19.5	99.7	±16.2	P > 0.05
	P < 0.05		P < 0.05		P < 0.05		
Serum B₂ microglob.							
Mild renal impairment gp	109.0	16.0	102.33	±19.25	105.67	±65.0	P > 0.05
Normal renal gp	110.44	11.84	108.44	±21.85	110.44	±17.4	P > 0.05
	P > 0.05		P > 0.05		P > 0.05		
Urinary albumin							
Mild renal impairment gp	5.20	2.50	71.10	±23.2	9.4	±3.9	P < 0.05
Normal renal gp	4.20	3.30	41.9	±28.9	8.4	±6.8	P < 0.05
	P > 0.05		P > 0.05		P > 0.05		
Urinary B₂ microglobulin							
Mild renal impairment gp	120.7	136.6	291.1	±284.0	371.3	±290.1	P < 0.05
Normal renal gp	95.1	83.0	387.0	±446.2	393.0	±361.8	P < 0.05
	P > 0.05		P > 0.05		P > 0.05		

Mild renal impairment group comprised 6 patients.

Normal renal group comprised 9 patients.

Table (9): Comparative analysis of serial changes in some renal function test among the thrombolytic group (Dyslepidemia versus non dyslepidemia subgroups).

Laboratory parameter	Admission valve		First day valve		Day 7 valve		Significance (F-test)
	MV	SD	MV	SD	MV	SD	
S.creatinine							
Dyslepidemic gp	1.42	±0.57	1.58	±0.980	1.20	±0.67	P > 0.05
Normal lipid gp	1.02	±0.36	1.08	±0.69	1.04	±0.84	P > 0.05
	P > 0.05		P > 0.05		P > 0.05		
Cr. clearance							
Dyslepidemic gp	100.4	±23.9	86.4	±17.8	90.5	±19.5	P > 0.05
Normal lipid gp	110.8	±18.3	86.2	±15.3	94.5	±18.3	P > 0.05
	P > 0.05		P > 0.05		P > 0.05		
Serum B₂ microglob.							
Dyslepidemic gp	109.0	±17.4	106.0	±23.6	112.1	±11.8	P > 0.05
Normal lipid gp	109.8	±10.9	103.3	±16.3	103.2	±16.3	P > 0.05
	P > 0.05		P > 0.05		P > 0.05		
Urinary albumin							
Dyslepidemic gp	4.16	±3.15	52.2	±28.03	7.76	±4.1	P < 0.05
Normal lipid gp	5.04	±2.22	56.7	±21.97	9.1	±4.6	P < 0.05
	P > 0.05		P > 0.05		P > 0.05		
Urinary B₂ microglobulin							
Dyslepidemic gp	105.3	±89.7	297.8	±234.9	332.13	±281.6	P < 0.05
Normal lipid gp	105.7	±106.7	379.0	±408.0	412.86	±364.4	P < 0.05
	P > 0.05		P > 0.05		P > 0.05		

Dyslepidemic group comprised 8 patients.
Normal lipid group comprised 7 patients.

Table (10): Correlation between the urinary albumin level and the urinary B2-microglobulin with some echocardiographic and labora... parameters among the thrombolytic group (n=15).

parameters	Urinary albumin level (24hr value)	Urinary B2-microglobulin level	
		24 hour value	Day 7 value
LV-ejection fraction	$r = +0.540$ $P < 0.05$	$r = +0.34$ $P > 0.05$	$r = +0.242$ $P > 0.05$
LV-percent fibrous shortening	$r = +0.637$ $P < 0.05$	$r = +0.416$ $P > 0.05$	$r = +0.346$ $P > 0.05$
Fasting blood sugar	$r = +0.243$ $P > 0.05$	$r = -0.109$ $P > 0.05$	$r = +0.094$ $P > 0.05$
CPK (peak value)	$r = 0.147$ $P > 0.05$	$r = -0.564$ $P < 0.05$	$r = +0.014$ $P > 0.05$
LDH (peak value)	$r = -0.509$ $P < 0.05$	$r = -0.565$ $P < 0.05$	$r = -0.164$ $P > 0.05$
S. createnin	$r = +0.104$ $P > 0.05$	$r = -0.247$ $P > 0.05$	$r = -0.387$ $P > 0.05$
Creatinine clearance	$r = +0.302$ $P > 0.05$	$r = +0.116$ $P > 0.05$	$r = +0.059$ $P > 0.05$

DISCUSSION

Renal glomerular function:

The present study showed that use of thrombolytic therapy produced transient glomerular impairment in the form of transient microalbuminuria (table 4 & Figure 3), although it did not produce any clinical proteinuria

Howe've'r Lynch & his associates (1995) (10), published that thrombolytic therapy had resulted in clinical proteinurina (urinary protein excretion > 0.15 gm/24h). in 82% of their studied patients. But, their estimation for proteinuria did not include admission sample (as in this study) which could delineate a certain percentage of their studied patients having proteinuria on admission (10). Also, they found proteinuria in 27% of their studied patient who received no thrombolytic therapy.

This later could be attributed to the higher age of their patients (mean 64 years) than in our studied patients (mean 48 years, table 1). Moreover, they did not exclude patients with renal failute .

Lynch & his associates (1995)(10) had reported also, that proteinuria related to streptokinase therapy had resolved by day 5 after infarction. The microalbuminuria in our studied patients was detected 24 hour after

thrombolytic therapy in 12 patients (80%) and disappeared completely on the 7th day of therapy (table 4 & Fig 3). This means that in both studies it was transient.

The occurrence of microalbuminuria among the different thrombolytic subgroups showed no difference in relation to the presence or absence of diabetes mellitus, hypertension, mild renal impairment as well as the presence of abnormal lipids (table 5).

Analysis of serial absolute values of urinary albumin excretion rate (in $\mu\text{g}/\text{min}$) among the whole thrombolytic group (table 4 & Fig 1) and different thrombolytic subgroups (tables 6-9) showed significant increase in urinary albumin excretion in 1st day after therapy than the admission and the 7th day values ($P < 0.05$, table 3). This means that thrombolytic therapy has resulted only in transient microalbuminuria and did not produce clinical proteinurina (all values were less than 150mg/day), and this effect has no relation to the presence of diabetes mellitus, hypertension, dyslipidemia or mild renal impairment.

The microalbuminuria observed among thrombolytic subgroups was

not associated with any changes in serum creatinine, creatinine clearance and serum B2-microglobulin. Microalbuminuria can also be associated with an acute phase response, in acute myocardial infarction (27), but the onset and resolution of the microalbuminuria was more rapid than in acute phase response. The small protein load contained in a bolus dose of streptokinase would be unlikely to cause proteinuria as a result of protein load (28). The excess microalbuminuria seen in the thrombolytic group could not be explained on the bases of acute myocardial infarction or its complications and/or differences between the thrombolytic and non-thrombolytic groups as all clinical and laboratory parameters were more or less similar at the start of myocardial infarction. The only difference is the use of streptokinase among the thrombolytic group. The non thrombolytic group on the other hand showed no microalbuminuria (table 3).

The use of intravenous streptokinase in acute myocardial infarction improved left ventricular performance and survival (29). The presence of significantly better left ventricular performance parameters (ejection frac-

tion (EF) and percent fractional fiber shortening (%FS), table 1) among the thrombolytic group could explain that better thrombolysis and reperfusion improve the left ventricular contractility (and help in wash out of thrombolytic end product into circulation). A significant positive correlation was found between the degree of microalbuminuria and left ventricular systolic functions parameters (EF, %FS) ($r = 0.54$ & 0.64 , $p < 0.05$ respectively) (table 10). From this it could be concluded that, the more successful the thrombolytic therapy and consequently improvement of global left ventricular function, the more is the degree of microalbuminuria. The concomitant increase in thrombolytic end products with efficient thrombolysis could be related to the pathogenesis and degree of transient microalbuminuria.

Microalbuminuria could be explained by complex mediated injury of the renal glomerular basement membrane and immune complex formation after streptokinase therapy in acute myocardial infarction (30) and serum sickness and renal injury (31). At the same time, this microalbuminuria can be explained by renal vascular injury due to cholesterol embolization syndrome (32).

Renal tubular function :

Although the urinary albumin excretion which reflect glomerular performance showed transient elevation after thrombolytic therapy, the urinary B₂-microglobulin which reflect renal tubular function showed progressive abnormal elevation after thrombolytic therapy as show in (table 4 and Fig 2 & 3).

The abnormal urinary B₂-microglobulin values of $> 370 \mu\text{g}/24 \text{ hr}$ was found in 5 patients (33.3%) receiving streptokinase by the 1st day of therapy and in 7 patients (44.66%) by the 7th day (table 4, $P < 0.05$). However no abnormal values was found among patients not receiving streptokinase therapy (table 3, $P > 0.05$).

No difference was observed as regard the abnormal urinary B₂-microglobulin among different thrombolytic subgroups (tables 5-9). This means that diabetes mellitus, mild renal impairment, hypertension or dyslipidemia did not alter the behaviour of tubular function to thrombolytic therapy.

The B₂-microglobulin is an endogenously produced substance with a molecular weight low enough to be fil-

tered completely across renal glomeruli. Nearly all the filtered B₂-microglobulin is actively reabsorbed by renal proximal tubular cells and catabolized during the reabsorptive process in the kidney tubules (33). If the reabsorption process by the renal tubules is disturbed, the majority of filtered B₂-microglobulin (100-200 mg/day) is excreted in the final urine (34).

The renal removal of low molecular weight protein, B₂-microglobulin, from serum encompasses three component mechanisms including glomerular filtration, tubular reabsorption and metabolism and excretion of the non reabsorbed protein with urine. Thus the urine concentration of B₂-microglobulin is dependent on the amount filtered by the glomeruli and on tubular reabsorption of this protein. Tubular reabsorption of B₂-microglobulin is normally about 99.9% of the filtered fraction and only about 0.1% is excreted in the urine, in which its concentration is maximally about $370 \mu\text{g}/24\text{h}$ (35). Concentration of B₂-microglobulin depends mostly on integrity of the proximal renal tubules and thus can be used in diagnosis and follow up tubular dysfunction (36).

The elevation of urinary B₂-

microglobulin observed among thrombolytic group can not be explained by neither the increase of its production, (which is endogenously constant), nor by any abnormal glomerular function (as creatinine clearance was within the normal range and the presence of normal serum B2-microglobulin level in whole thrombolytic (table 4) and all subgroups (tables 6-9). Thus, the abnormal urinary B2-microglobulin values ($>370 \mu\text{g}/24\text{hr}$) found in 5 patients with thrombolytic therapy by 1st day and in 7 patients on the 7th day could be attributed to impaired tubular reabsorption after thrombolytic therapy and this was probably not be related to the hemodynamic changes during acute myocardial infarction as it did not present among any patient not receiving thrombolytic therapy.

The impaired tubular reabsorption after thrombolytic therapy could be explained by the abnormal haemorheology of blood and formation of immune complexes as well as the massive production of fibrinolytic products after successful lysis of intracoronary microthrombi. Also, cholesterol embolization syndrome may have some role. The increased incidence of abnormal urinary B2-microglobulin on the 7th than the 1st day after thrombo-

lytic therapy (46.6% versus 33.3% $P > 0.05$, table 4), although non significant, but may suggest that the impaired tubular reabsorption is related more to immune complex deposition.

Significant negative correlation was found between urinary B2 microalbumin and peak CPK ($r = -0.56$, $p < 0.05$) and LDH ($r = -0.57$, $P < 0.05$) (table 10). This signifies that the increase in B2-microglobulin was inversely related to infarct size and so the degree of tubular injury after thrombolytic therapy is reversely related to infarct size. This means that B2-microglobulin is related to effective thrombolysis; opening of occluded vessel, preserving myocardium and consequently left ventricular performance as well as wash out of the thrombolysis end products which could produce the impaired renal tubular function.

In Conclusion : Thrombolytic therapy has resulted in transient (glomerular dysfunction) in the form of microalbuminuria by the 1st day after therapy and resolved completely by 7th day. This microalbuminuria was not related to the presence of diabetes mellitus, hypertension, mild renal impairment or dyslipidemia, but

correlated positively with the success of thrombolysis and improvement in global systolic left ventricular functions.

Thrombolytic therapy has resulted in abnormal renal tubular function which started by 1st day after therapy and persisted on the 7th day. This abnormal tubular function was not related to the presence of diabetes mellitus, hypertension, mild renal impairment or dyslipidemia, but correlated with effective thrombolysis.

Thrombolytic therapy can be used safely (unless there is other contraindication) among patients with diabetes mellitus, hypertension, dyslipidemia as well as the presence of mild renal impairment.

A follow up study to the residual effect of thrombolytic therapy on renal tubular function should be looked for to evaluate the course of this abnormal urinary B2-microglobulin values.

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دراسة وظائف الكلى بعد العلاج بمذيبات الجلطة فى

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يعتبر دواء مذيب الجلطة (الاستريبتوكاينيز) من الأدوية الأساسية فى علاج مرضى احتشاء القلب الحاد أثناء الساعات الأولى بعد حدوث الجلطة وهو يؤدى إلى تحليل الفيبرينوجين الداخلى فى تكوينها .

يستهدف هذا البحث دراسة التغيرات التى قد يحدثها إستخدام دواء الاستريبتوكاينيز على وظائف الكلى الترشيحية (وظائف حليمات الكلى)، والإخراجية (وظائف أنابيب الكلى) .

وقد اشتملت هذه الدراسة على عدد ٣٠ مريضاً يعانون من مرضى احتشاء عضلة القلب الحادة بوحدة العناية المركزة بمستشفى الطوارئ الجامعى بالمنصورة - تم تقسيمهم إلى مجموعتين حسب العلاج المعطى لكل مريض :

(أ) المجموعة الأولى : ومكونة من عدد ١٥ مريضاً شمل علاجهم إعطاء دواء الاستريبتوكاينيز وذلك لوجود موانع خاصة لاستخدام هذا الدواء فى هؤلاء المرضى).

(ب) المجموعة الثانية : ومكونة من عدد ١٥ مريضاً شمل علاجهم إعطاء الاستريبتوكاينيز وقد تم تقسيمهم إلى عدة مجموعات حسب وجود مرض البول السكرى - مرض إرتفاع ضغط الدم - وجود زيادة فى دهون الدم وكذلك وجود نقص طفيف فى معدل استخلاص الكرياتينين (أقل من ٨٠ سم³/دقيقة).

وقد تم عمل المتابعة الصحية والفحوصات المعتادة لهؤلاء المرضى خلال وجودهم بالعناية المركزة أثناء فترة العلاج وإجراء البحث (انزيمات القلب - صورة الدم - سرعة الترسيب - وظائف الكبد - سكر الدم - تحليل البول - رسومات القلب - الاشاعات السينية وفحص القلب بالموجات فوق الصوتية) .

وقد تم عمل فحوصات معملية متكررة خاصة بهذا البحث فور دخول المريض العناية المركزة قبل بدء العلاج (اليوم الأول)، وفى اليوم التالى لأخذ العلاج وكذلك فى اليوم السابع من بدء العلاج وشملت :

(أ) تحاليل معملية لتقييم وظائف حليمات الكلى (الوظائف الترشيحية للكلى) وشملت :

- كرياتينين الدم - معدل استخلاص الكرياتينين .

- نسبة إخراج الألبومين بالبول (وتعيين وجود الميكرو البومينوريا) .

(ب) تحاليل معملية لتقييم وظائف أنابيب الكلى (الوظائف الإخراجية للكلى) وشملت

- مستوى البيتا-٢ ميكروجلوبولين بالدم. - مستوى البيتا-٢ ميكروجلوبولين بالبول .

وقد أظهرت النتائج مايلي :

أولا : المرضى الذين لم يشمل علاجهم إعطاء دواء الاستيرينوكاينيز : لم يوجد هناك أى تغييرات معملية تشير إلى خلل فى وظائف الكلى أثناء فترة العلاج.

ثانياً : المرضى الذين شمل علاجهم إعطاء دواء الاستيرينوكاينيز لوحظ :

(أ) زيادة مؤقتة فى نسبة إخراج الألبومين بالبول وحدوث الميكروالبومينوريا فى اليوم الأول فقط وتزول عند اليوم السابع من بدء إعطاء العلاج .

(ب) زيادة تصاعدية فى مستوى البيتا -٢ ميكروجلوبولين بالبول فى اليوم الأول وتستمر الزيادة حتى اليوم السابع من بدء إعطاء العلاج .

(ج) عدم وجود أى تغييرات فى مستوى كرياتينين الدم - معدل إستخلاص الكرياتينين ومستوى البيتا-٢ ميكروجلوبولين بالدم .

(د) وجود علاقة ارتباطية موجبة بين درجة الميكرو البومين فى البول ووظائف البطين الأيسر .

(هـ) وجوب علاقة ارتباطية سالبة بين مستوى البيتا-٢ ميكروجلوبولين بالبول انزيمات القلب .

(و)عدم وجود فرق فى التغيرات المعملية التى ظهرت نتيجة وجود مرض البول السكرى - مرض ارتفاع ضغط الدم - زيادة نسبة دهون الدم أو وجود نقص طفيف فى معدل إستخراج الكرياتينين بين المرضى.

وقد خلصت الدراسة إلى :

- عمل دراسة ممتدة (متابعة) لمتابعة التغيرات التى يحدثها إستخدام دواء الاستيرينوكاينيز على وظائف أنابيب الكلى .

- يمكن إستخدام دواء الاستيروكلين بأمان فى مرضى البول السكرى - مرضى ارتفاع ضغط الدم - مرضى زيادة دهون الدم ومرضى قصور وظائف الكلى (مالم يكن هناك أى موانع أخرى).

بسم الله الرحمن الرحيم

الحمد لله الذي هدانا لهذا

الذي كنا لنهتدي لاهل

الهدى والحمد لله الذي هدانا لهذا

الذي كنا لنهتدي لاهل الهدى

والحمد لله الذي هدانا لهذا

الذي كنا لنهتدي لاهل الهدى

والحمد لله الذي هدانا لهذا

الذي كنا لنهتدي لاهل الهدى

والحمد لله الذي هدانا لهذا

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والحمد لله الذي هدانا لهذا

الذي كنا لنهتدي لاهل الهدى