



ISSN NO. 2320-5407

Journal homepage: <http://www.journalijar.com>
Journal DOI: [10.21474/IJAR01](https://doi.org/10.21474/IJAR01)

INTERNATIONAL JOURNAL
OF ADVANCED RESEARCH

RESEARCH ARTICLE

Effect of oral Hypertensive agents on Biochemical parameters in Diabetic patients : In vivo study.

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Manuscript Info

Manuscript History:

Received: 14 February 2016
Final Accepted: 19 March 2016
Published Online: April 2016

Key words:

Antihypertensive drug, Diabetes mellitus, Captopril, Atenolol, Biochemical parameters.

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Abstract

Objectives: In vivo study was carried out to monitor the effect of antihypertensive drugs (Captopril and Atenolol) on the metabolites and enzymes that are requested for professional diagnosis in diabetic patients.

Methods: 30 hypertensive diabetic subjects of type II (18 males and 12 females) with an average age of (55 ± 15 years) and average weight (61 ± 16.5 kg) were participated in this study. 17 subjects were on Captopril therapy (50mg/daily) and 13 subjects were on Atenolol therapy (50mg/daily). 30 healthy volunteers of comparable age (52 ± 15 years) and an average weight (85.5 ± 15.5 kg) was used as control sample. Two venous blood samples were collected from each subject, first blood sample was taken before drug therapy and the second blood sample was taken three weeks after drug therapy.

Results: Captopril therapy significantly elevated Total protein (TP), Creatinine, Total cholesterol, Triglyceride, and Creatine kinase (CK) whereas Total bilirubin (T.bil.) was significantly reduced. Total cholesterol (T.Chol.), Triglyceride (TG) and Alanine transaminase (ALT) were found significantly increased in patients with Atenolol therapy.

Conclusion: Among the antihypertensive drugs, Atenolol has less effect on all biochemical laboratory parameters and therefore it is more favorable than Captopril.

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Introduction:-

The effects of antihypertensive agents on laboratory findings have been evaluated. Antihypertensive reagents that act as Angiotensin-converting enzyme (ACE) inhibitors and beta blockers are neutral that have less effect on most of laboratory findings (Mohammed and Wahda. 2013; Jabar. 2009). The choice of antihypertensive drugs should be determined by its capacity to lower blood pressure effectively and to protect the patient's kidneys from ongoing injury and its side effects. Patients with diabetes mellitus have a high risk of cardiovascular disease. Treatment of risk factors and morbidities, such as hypertension, is very important and may effectively prevent cardiovascular events. In combination treatment, a blocker of the renin-angiotensin system should be included and probably be the first choice (Aksnes et al. 2012). Some studies such as (Ibrahim and Al-Joudi. 2009; Badar et al. 2011) reported that captopril and atenolol are used as first line therapy for blood hypertension because of their minor side effects. However captopril therapy was investigated largely more than atenolol. There are contradictory reports about the impact of these antihypertensive drugs in terms of their effect on laboratory findings. Dunder et al.(2003) and Padwal et al. (2004) recorded an increase in glucose concentration in patients when using 100 mg of captopril while other studies (and Thomas . 2006; Ibrahim et al. 2010) have not recorded any effect of captopril and atenolol on glucose level. On the other hand Whelton et al. (2005) reported a significant decrease in the concentration of fasting glucose after antihypertensive treatment. An elevation of lipid profile after 24 weeks of treatment with atenolol and number of side effects have been reported with atenolol and captopril (Whelton et al. 2005). Isam and Nada (2013) noted small but significant reduction in serum lipid levels after captopril therapy. On contrary triglycerides and cholesterol was remained unchanged in Gonzalez et al. (1991) study. Badar et al. (2011) showed significant increase in mean blood sugar and lipid profile after 24 weeks of atenolol therapy. The liver enzymatic activities alanine

transaminase (ALT) and aspartate transaminase (AST) were also affected by the captopril treatment. The AST levels were mildly increased in both pre- and post-treatment samples in comparison with the control subjects (Forné et al. 2007; Giannini et al. 2005). The creatine kinase activity was increased in hypertensive patients after treatment with captopril drug (Warden et al. 2014). The level of total bilirubin was increased in patients receiving captopril therapy (Shane and Elizabeth. 2014). Less impact of captopril therapy on bilirubin level was reported by Schattner et al. (2001). However, Siest et al. (2001) reported an increase in creatinine and urea levels with captopril therapy. Chrysochou et al. (2012) reported that urinary protein excretion was decreased by about 48% and creatinine clearance remained unchanged after captopril therapy. In this study both antihypertensive drugs captopril and atenolol have been used to investigate their effect on some laboratory findings.

Materials and Methods:-

In vivo study:-

This study was conducted on 30 diabetic patients of type II (18 males and 12 females). Their ages range from (55 ± 15 years) and average weight (61 ± 16.5 kg). The patients were newly diagnosed with essential hypertension in the outpatient clinic of Jordan hospital. The patients were divided into two groups, according to the drug therapy. One group (11 males and 6 females) was on antihypertensive drug Captopril (50mg/daily). The other group (7 males and 6 females) was on Atenolol therapy (50mg/daily). Thirty healthy volunteers of comparable age (52 ± 15 year) and an average weight (85.5 ± 15.5 kg) matched with the first group by age, sex, and BMI (weight in kg) were used as control sample.

Blood samples:-

Two venous blood samples were obtained from each subject participated in this study. First blood sample was taken before drug therapy and the second blood sample was taken three weeks after drug therapy. All blood samples were left to clot and were centrifuged at 3500 rpm for 10 minutes. Serum obtained from each sample was used to measure the biochemical parameters involved in this study.

Biochemical parameters determination:-

All kits used to measure the biochemical parameters (Glucose, Total protein, Creatinine, Total cholesterol, Triglyceride, Total bilirubin, Alanine transaminase, Creatine kinase) involved in this study were purchased from Randox laboratories. Ltd; UK) and all measurements were carried out according to methods prescribed by Burtis et al. (2014).

Results:-

The effect of antihypertensive agents Atenolol and Captopril on laboratory findings are listed in table 1 and 2 respectively. In table (1), Atenolol therapy does not show any effect on the level of glucose, Creatinine, total protein, Total bilirubin and CK compared with both pre-treated patients and control subjects ($p > 0.05$). Total cholesterol and triglyceride were found significantly increased ($p < 0.05$) in atenolol post-treated patients compared with the control subjects. There was a significant increase in the activity of ALT ($p < 0.05$) in atenolol post-treated patient compared with the control and the pre-treated patients (table 1).

Table 1. In vivo effect of Atenolol on laboratory findings.

Biochemical parameter/unit	Control ± SD		Pre-treatment ± SD		Post-treatment ± SD		M1	M2	M3
Glucose (mg/dl)	97.1	6 17.34	145.34	19.12	153.60	15.23	NS	NS	NS
TP g/dl	74.32	8.43	77.80	5.41	73.40	11.96	NS	NS	NS
Creatinine (mg/dl)	1.12	0.25	1.14	0.14	1.22	0.17	NS	NS	NS
T.Chol. (mg/dl)	191.43	34.29	218.90	56.78	244.40	67.77	NS	NS	*
TG (mg/dl)	123.06	32.94	183.90	125.95	257.50	153.64	NS	NS	*
T.Bil (mg/dl)	0.63	0.11	0.73	0.30	0.66	0.24	NS	NS	NS
ALT (U/L)	18.37	6.36	15.70	3.11	19.10	2.19	NS	NS	*
CK (U/L)	131.75	33.91	120.60	31.24	124.40	44.30	NS	NS	NS

* Significant ($p < 0.05$), NS = non-significant ($p > 0.05$)

M1 = control with pre-treatment , M2 = pre-treatment with post-treatment , M3 = control with post-treatment. Total protein (TP), Total cholesterol (T.Chol.), Triglyceride (TG), Total bilirubin ALT (alanine Tranaminase) , Creatine kinase (CK).

50mg daily of Captopril therapy affects most of the laboratory parameters involved in this study (table 2). Total protein, Creatinine levels were found significantly increased ($p < 0.05$) in post-treated patients compared with pre-treated patients and the control subjects. Total cholesterol and triglyceride levels were found significantly elevated ($p < 0.05$) in post-treated patients compared with the control subjects. Table (2) demonstrates that captopril caused a significant decrease in total bilirubin concentration in comparison to the post- treated and post-treated patients and control group ($p < 0.05$). The data recorded in table 2 showed that the activities of ALT and CK were found significantly elevated ($p < 0.05$) in Captopril post-treated patients compared with the pre-treated patients.

Table2. In vivo effect of Captopril on laboratory findings.

Biochemical parameter/unit	Control \pm SD		Pre-treatment \pm SD		Post-treatment \pm SD		M1	M2	M3
Glucose (mg/dl)	95.53	16.42	138.82	17.35	142.50	16.50	NS	NS	NS
TP g/dl	75.75	5.43	71.80	8.66	85.70	5.37	NS	*	*
Creatinine (mg/dl)	0.83	0.25	1.10	0.11	1.33	0.13	NS	*	*
T.Chol. (mg/dl)	201.43	43.29	221.40	51.61	231.10	48.36	NS	NS	*
TG (mg/dl)	113.06	32.91	132.00	56.33	219.70	43.62	NS	*	*
T.Bil(mg/dl)	0.81	0.12	0.92	0.20	0.43	0.13	NS	*	*
ALT (U/L)	15.37	2.32	16.30	3.41	21.00	3.34	NS	NS	*
CK (U/L)	104.72	18.83	94.22	31.43	135.12	21.62	NS	NS	*

* Significant ($p < 0.05$), NS = non-significant ($p > 0.05$)

M1 = control with pre-treatment , M2 = pre-treatment with post-treatment , M3 = control with post-treatment. Total protein (TP), Total cholesterol (T.Chol.), Triglyceride (TG), Total bilirubin ALT (alanine Tranaminase) , Creatine kinase (CK).

The results were expressed as the mean \pm SD. A student T-test was used to examine the difference in the mean of the parameters tested. The p value of less than 0.05 was considered as significant.

Discussion:-

The antihypertensive drugs used in this study were captopril (50mg daily) which acts as angiotensin converting enzyme inhibitors (ACEIs), and atenolol (50mg daily) that belongs to a class of drugs known as beta blockers. The comparison between the concentrations of the biochemical parameters in diabetic patients before and after drug treatment would give an obvious measure of the effect of any drug on such biochemical parameters. The effect of these drugs on some laboratory tests report contradictory results in previous studies. The present study shows that glucose was not affected by atenolol which disagrees with Maritz et al. (1995) that atenolol decreases insulin sensitivity therefore increasing insulin resistance, on the other hand Giugliano et al. (1997) reported that glucose level decreases on captopril over 12 weeks of treatment while Donovan et al. (2003) found that captopril had no significant effect on basal plasma insulin level .The captopril is found to have more profound impact on the laboratory findings involved in the study.

Atenolol was found to elevate the hepatic enzyme ALT compared with post-treatment patients which may be due to the induction of hepatic microsomal enzyme. This study shows that 50mg daily of captopril therapy does not affect ALT activity which agrees with the result obtained by Mohamad andWahda. (2013) and disagrees with the result obtained by Rahmat et al. (2000).However this difference in response to antihypertensive agents in vivo depends on the physiological response by the patient himself. Increase in creatinine levels with captopril therapy may be due to biological effects, as reported by in previous studies (Siest et al.,2001 and Robert, 2010).This study found that the use of captopril in hypertensive patients has resulted in a significant reduction of mean total bilirubin level, which was in accordance with the results of Rahmat et al; (2000) who reported that most hepatic toxicity caused by captopril is mild and transient and the elevation in the serum ALT and AST activities is mild and resolved after discontinuation of the therapy. This mild cellular damage may be attributed to the accumulation of toxic metabolite of the drug within the hepatocytes causing direct injury or indirect injury by immune mediated cellular damage

(Bonacini and Miyashita; 2002). The elevation in serum ALT activity suggested that captopril may have mild to moderate cholestatic effect on the liver (Rahmat et al., 2000). Both drugs investigated in the present study caused an increase the level of lipid profile which consistent with result obtained by previous reporters (Maritiz; et al. 1995; Ibrahim et al. 2010) this may be explained by their impact directly on lipid metabolism. Galcerá. et al (2001) reported that using atenolol and captopril have protective effect on myocardium. In the present study CK was found significantly increased on captopril therapy which contradicts the results reported by (Xiangmin, 2014).

Conclusion:-

One side effect of antihypertensive drugs is their impact on biochemical molecules and their metabolism. The purpose of this study was to assess the effect of commonly used antihypertensive drugs so called captopril and atenolol on biochemical parameters. The results presented in this study demonstrated that some of laboratory findings are clearly altered.

Atenolol has less effect on all biochemical parameters involved in this study that can be considered as more favorable than captopril regarding its effect on biochemical parameters.

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