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Full Length Research Paper

Captopril interferes with some serum biochemical findings

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Captopril is a widely used anti-hypertensive drug that acts by inhibiting angiotensin-converting enzyme. This work has been carried out to investigate the effects of captopril on some common biochemical laboratory parametres in the sera of patients receiving the drug. For this study, 40 subjects were included, all within the age range of 40 to 63 years and with newly diagnosed essential hypertension. From each patient, two samples were taken, one immediately before the start of treatment and the second one taken two weeks later. The control group comprised 30 apparently healthy volunteers of comparable ages and genders. The biochemical parameters measured in the sera were glucose, total protein (TP), urea, creatinine, total cholesterol (TC), triglycerides (TG), liver enzymes and creatine kinase (CK). Captopril exerted significant increases in the obtained readings for the concentrations of glucose, TP, urea, creatinine, TC, TG, AST and LDH. The increases in readings in the biochemical parameters may be attributable to chemical or to physical interactions. They could also be induced by physiological, enzymatic or by *IN VIVO* metabolic factors. By all means, these alterations that accompany captopril treatment must be taken into account by physicians and laboratory workers, to help avoid misinterpretation of laboratory data.

Key words. Captopril, biochemical laboratory tests, drug interactions.

INTRODUCTION

Drug interactions with laboratory findings have been reported previously. Examples of such interactions are the widely used aspirin and ascorbic acid, both which could interfere with serum readings to give a state of false hyperglycaemia (Young et al. 1972). Captopril, D-3-mercapto-2-methyl (propanoyl-L-proline, 1), is a selective inhibitor of angiotensin I-converting enzyme (ACE) (Cushman et al., 1978; Schmidt et al., 1986). It exerts vasodilatory effects and enhances the renal excretion of sodium (Chrysant et al., 1985; Hauger Kleven, 1985; Hymes et al., 1983; Matcher et al., 2008; Sleight, 2001; Zanchetti et al., 2006), hence, it is mostly used in hypertension and in cardiac conditions such as post-myocardial infarction or congestive heart failure. It is also used in the preservation of kidney function in diabetic nephropathy and in cancer therapy (Lindberg et al., 2004). It has been estimated that more than 75% of the drug is rapidly absorbed in the gastro-intestinal tract and partially metabolized to produce inactive mixed disulfides with endogenous thiol compounds. Both metabolites and unchanged captopril are excreted in the urine. The half-life of captopril in the circulation is about 1.9 h in healthy volunteers (Romankiewicz et al., 1983). Although hepatotoxicity of ACE inhibitors has been rarely reported (Yeung et al., 2003), captopril toxicity, in particular, is even lower (DiBianco, 1986; Sebates et al., 2007). Nevertheless, the effects of captopril on chemical pathology data have not been disclosed. This work was performed to study the effects of captopril on some

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Abbreviations: TP, Total protein; **TC,** total cholesterol; **TG,** triglyceride; **AST,** aspartate aminotransferase; **ALT,** alanine aminotransferase; **LDH,** lactate dehydrogenase ; **CK,** creatine kinase.

Table 1. The *In vivo* effects of captopril on the serum biochemical parameters.

Parameters	Control	Pre-treatment	Post-treatment	M1	M2	M3
Glucose mg/dl	93.562± 18.402	96.80 ± 19.309	108.80± 33.508	NS	NS	NS
TP g/l	75.75± 8.434	73.80± 9.908	82.70± 6.377	NS	*	*
Urea mg/dl	32.6± 10.9	30.5 ± 5.9	36.9 ± 11.19	NS	NS	NS
Creatinine mg/dl	1.113± 0.255	1.088± 0.119	1.336 ±0.276	NS	*	*
TC mg/dl	191.437± 34.298	219.40± 51.631	226.10± 48.363	NS	NS	*
TG mg/dl	123.06± 32.947	196.20 ± 116.331	219.70 ± 153.629	NS	NS	*
AST U/l	22.937 ± 6.884	31.60± 9.167	31.50± 9.594	*	NS	*
ALT U/l	18.375 ± 6.365	14.30± 8.124	17.60± 8.487	NS	NS	NS
CK IU/l	130.50± 33.091	124.90± 26.568	156.30± 26.853	NS	NS	*
LDH U/l	131.75± 33.914	92.20 ± 33.568	101.10± 37.625	*	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

common biochemical pathology tests.

PATIENTS AND METHODS

The *in vivo* tests were conducted on the sera of forty patients newly diagnosed with essential hypertension (23 females and 17 males) selected and recruited for the study at Dr. Abdul-Majeed Hospital, Baghdad. To perform the work, ethical approval was granted by the Pharmacy School Heads of Departments meeting in October 2002 and all patients were informed of the objectives of work in advance. The patients' ages ranged from 40 to 63 years and they were all given 25 mg of captopril daily for two weeks. Pre-treatment venous blood samples were collected from each patient and post-treatment blood samples were collected two weeks after the beginning of the treatment. Serum was obtained after centrifugation of the clotted blood. Serum samples from thirty healthy subjects were used as controls. Control subjects were with no evidence of hypertension and diabetes mellitus and with ages (ranging from 35 to 67 years) and genders selected to match those of the test subjects. The biochemical parameters measured included glucose, total protein (TP), urea, creatinine, total cholesterol (TC), triglyceride (TG), aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH) and creatine kinase (CK). These parameters were measured by using Randox kits (Randox Laboratories Ltd., United Kingdom) and read by spectrophotometry.

Statistical analysis

The results were expressed as the mean 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 significant. ANOVA was used to evaluate the effects of different concentrations of the drug on the biochemical parameters.

RESULTS

The *IN-VIVO* effects of captopril on the biochemical parameters

Following captopril therapy, considerable increases in the readings of all biochemical parameters were obtained. Although all test parameters of the post–treatment sera were raised compared with both the pre-treatment samples and the control samples, the rise of the TG reading was more sharp than the others. Moreover, the elevations in the concentrations of TP and of creatinine were significant in comparison with both the control and pre-treatment sera (Table 1).

The effect of captopril on enzymatic activities

The enzymatic activities 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. The CK activity levels were increased in post-treatment samples, yet they were decreased in the pre-treatment samples. The LDH activity levels were reduced in both pre- and post-treatment sera in comparison with samples of the control subjects (Table 1).

DISCUSSION

Although the growth in therapeutic drugs has resulted in considerable progress in the treatment of diseases, side effects have been reported in many of them, including drug interactions (Young et al., 1972). Since anti-hypertension drugs are long life drugs, then, influences of drug therapy on laboratory results need monitoring to avoid more serious consequences and occasionally, erroneous therapeutic decisions (Hansten, 1979).

In a recent study, captopril was found to exert some chemical or physical interferences in measurements of some serum analytes *in vitro* and it also suggested the necessity of performing this *in vivo* work (Ibrahim and Al-Joudi, 2009).

Interference by endogenous or exogenous substances with assay techniques is a common problem in the

clinical laboratory. However, increases in creatinine and urea levels with captopril therapy may be due to biological effects, as reported previously (Cirillo et al., 1988; Hirakata et al. 1984; Salway 1998; Siest et al., 1988; USP drug information for health care professional, 2001). Total protein was increased with captopril and this effect is not likely to be of metabolic origin, since it would probably take a longer time and justifiable biological stimulation to increase the protein content. So it is more likely to attribute that increase to physical or chemical interferences. The levels of TC and TG were significantly altered by captopril therapy, while captopril has been reported to improve endothelium-dependent coronary vasodilatation in patients with atherosclerosis (Fogari and Zoppi, 1999; Oskarson and Heistad, 1997), implying that TC and TG increases may be due to mobilization of fats deposited in endothelia of arteries.

The results presented in this study demonstrated clearly that some laboratory findings are altered the drug. The *in vivo* alterations in the reading of concentrations of metabolites and enzymes may be, in part, due to pharmacodynamic activities besides physical and chemical factors. However, the impact of these various factors cannot be measured separately from this current work. When drugs are detected as interfering with laboratory results, the test may have to be repeated or the laboratory personnel may need to perform special procedures to eliminate or adjust the interference. Furthermore and among other unwanted findings, the effects on the compositions of body fluids are likely to be more apparent when large doses of a drug are administered for a long-term than administration with a single dose (Ibrahim and Al-Joudi, 2009).

Although many drug-related problems come up unexpectedly and can not be predicted, a few problems are related to known pharmacological actions of the drugs and can reasonably be anticipated.

Conclusions

As drug therapy becomes more complex and as the number of individuals being treated with two or more drugs simultaneously, may increase, the ability to predict the magnitude of a specific action of any given drug diminishes. These circumstances point at the need, not only for keeping medication records for patients, but also for closer monitoring and supervision of drug therapy so that unanticipated problems can be prevented, or detected at an early stage in their development. Furthermore, alterations due to drug interference must be taken into account by physicians to avoid misinterpretation of laboratory data.

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