DISCREPANCIES IN DIGOXIN DETECTION BY FLUORESCENCE POLARIZATION IMMUNOASSAY

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ABSTRACT

Digoxin is the most widely prescribed cardiac glycoside. The therapeutic use of this digoxin derivative is constrained by its narrow therapeutic range, 0.8 to 2.0 ng per ml of serum. Its toxic effects are generally seen at concentrations in serum above 2.5 ng /ml. Therapeutic drug monitoring of digoxin concentration is valuable in reducing the incidence of digoxin toxicity due to intentional or unintentional overdoses. This study was done on fourty five blood samples from patients aged from 1 month to 90 years of different medical conditions (11 patients had hypertrophic cardiomyopathy with heart failure, 19 were healthy, two were diabetic ,one had congestive heart failure, one had chronic renal failure ,two had liver cirrhosis with heart failure and nine had congenital heart disease with heart failure) to evaluate discrepancy between estimated total (protein binded) digoxin level, actual (free) digoxin level, and the clinical picture of the patients. Digoxin level was measured by TDx analyzer in Poison Laboratory at Emergency Hospital, Mansoura University. It was done before and after ultrafiltration with millipores centrifree micropartition device. The digoxin level with ultrafiltration was lower than the level without ultrafiltration in patients totally. This was significant (P= 0.005) between groups with Anova test. It was highly significant with one paired t- test in patients with cardiomyopathy , patients with congenital heart disease (P< 0.001) and least statistical significant in heart failure with liver cirrhosis (P= 0.026).There was statistical significance between digoxin level in patients presented with tachycardia (P< 0.001) and patients with bradycardia (P= 0.006).No Statistical significance with other manifestation like visual and gastrointestinal (GIT). In conclusion, digoxin levels which are measured by immunoassay method must be interpreted carefully in patients with some medical conditions like congenital heart disease with heart failure, cardiomyopathy, neonates, liver cirrhosis and remeasured after ultrafiltration especially when it is not coincided with the clinical picture and estimation of digoxin level by High Performance Liquid Chromatography (HPLC) is recommended in presence of cardiac manifestations in the pervious mentioned medical conditions and in cases of digoxin toxicity to detect FAB antibodies dose precisely.

INTRODUCTION

Cardiac drugs are primarily used for treatment of angina, arrhythmias, and congestive heart failure. Digoxin is the most widely prescribed and therapeutically monitored. Several reasons make measurement of cardiac drugs in serum important: their narrow therapeutic index, similarity in clinical complications and presentation of under - and overmedicated patients, need for dosage adjustments, and confirmation of patient compliance (Roland et al., 1998).

Although several methods have been used for measuring digoxin in biological fluids, immunoassay is the prominent method currently used. However, because of measurement interferences caused by endogenous and exogenous substances, overlap between toxic and non toxic concentrations and a narrow therapeutic index, the therapeutic monitoring of digoxin continues to have substantial difficulties. Thus, evaluation of digoxin immunoassay methods for cross-reactivity of endogenous substances (digoxin-like immunoreactive substances) that can cause false positive results is important (Jortani and Valdes, 1997). Digoxin like immunoreactive factors (DLIFs) are endogenous steroid like compounds structurally related to the plant - derived cardiac glycoside "digoxin" (Hassan et al., 1996). DLIFs cross react with antidigoxin antibodies and falsely elevate serum digoxin concentrations, interfering in interpretation of results for therapeutic digoxin monitoring and falsely lower digoxin values have been reported (Amitava, 2002).

AIM OF THE WORK

This study was done on fourty five blood samples to evaluate discrepancy between estimated total (protein binded) digoxin level, actual (free) digoxin level and the clinical picture of the patients.

SUBJECTS AND METHOD

The subjects were 45 patients, aged from 1 month to 90 years, 15 females and 30 males ; two patients were accidental digoxin intake, 19 were suicidal intake and 24 were on digoxin therapy for congestive heart failure. 11 patients had hypertrophic cardiomyopathy with heart failure, 19 were healthy, two were diabetic, one had congestive heart failure, one had chronic renal failure ,two had liver cirrhosis with heart failure and 9 had congenital heart disease with heart failure. Blood samples were obtained from all patients, centrifuged and digoxin was measured by Abbott fluorescence polarization immunoassay (TDx analyzer which was developed by Abbott laboratories, USA) according to Digoxin Assay II - method in the Abbott manual of Abbott Diagnostic division of

Abbott Laboratories in Poison Laboratory at Emergency Hospital, Mansoura University. The normal therapeutic range for digoxin in the laboratory is 0.5 - 2 ng/ml.

Total serum bilirubin was measured according to method of Tietz,(1995) and serum creatinine was measured according to method of Henry, (1974). The patients were assessed by their clinical picture by which they were presented to the hospital like cardiac, visual and gastrointestinal manifestations.

The digoxin level of these patients was detected in the serum without filtration (total digoxin) then analyzed after ultrafiltration of the samples (free digoxin) and interpreted in relation to the patients clinical picture and medical condition. Protein-free ultrafiltration was done by centrifuging the samples at 20,000 rpm., then ultrafiltration by millipores centrifree micropartition device (membrane filter) according to method of Ujhelyi, (1992).

The statistical analysis of data was done by using Excel program and SPSS program (Statistical Package For Social Science version 10). The description of data was done in the form of mean ± SD for quantitative data and frequency and proportion for qualitative data.

The analysis of data was done to test statistical significant difference between groups. For qualitative data (frequency and proportion) Chi-square test was used. For quantitative data (mean ± SD) was done. Student t-test was used to compare between two groups. Paired t-test was used to compare one group at different times. One way Anova test was used to compare between more than two groups. To test association between variables correlation Co-efficient test was used. P is significant if ≤ 0.05.

RESULTS

Tables (1) and (2) show statistical data of age, sex , clinical and laboratory details of patients presented to Poison Unit at Emergency Hospital, Mansoura University. They were 45 patients 30 male (66.7%) and 15 females (33.3%). They aged from minimum (1 month) to maximum (90 years) with mean ± SD (32.61 ± 27.42). They were of different medical conditions like congestive heart failure with myopathy: n. 11 (24.4%); healthy: n.19 (42.2%); diabetes: n.2 (4.4%); congestive heart failure: n.1 (2.2%); chronic renal failure: n.1 (2.2%), heart failure with liver cirrhosis: n.2 (4.4%); congenital heart disease with heart failure: n.9 (20%). Their bilirubin ranged from 0.3 to 6.2 mg/ 100 ml (1.30 ± 1.36) and creatinine ranged from 0.3 to 5.50 mg/ 100ml (1.36 ± 1.16).

Table (3) shows mode of digoxin intake.

24 patients (53.3%) took digoxin as therapy, 19 patients (42.2%) took digoxin suicidally, and 2 patients (4.4) took digoxin accidentally.

Table (4) shows cardiac manifestations of the patients; 23 (51.1%) presented with tachycardia, 20(44.45) presented with bradycardia, 2 patients (4.4%) had no cardiac manifestations.

Table (5) shows visual and gastrointestinal (GIT) manifestations of the patients; 28 patients (62.2%) had visual manifestations in the form of: yellow halos around lights , blurred vision and scotomata and 17 patients (37.8%) had no visual manifestations, 37patients (82.2%) had GIT manifestations in the form of: nausea and vomiting and 8 patients (17.8%) had no manifestations.

Table (6) shows statistical data of digoxin level without ultrafiltration and with ultrafiltration in the different medical conditions. Digoxin level without ultrafiltrafiltration ranged from 4.36 - 12.34 mg/ml with mean ± SD (7.48 ± 1.86). Digoxin level with ultrafiltration ranged from 1.30 - 10.44 ng/ml with mean ± SD (5.64 ± 2.06) and has highly statistical significance (P = 0.005) with Anova test. Digoxin level much decreased with ultrafiltration than without ultrafiltration in the following medical conditions: congestive HF with myopathy, diabetes, congestive HF, chronic renal failure, HF with liver cirrhosis and congenital heart disease with H.F. In healthy persons the level didn't change significantly.

Table (7) shows relation between digoxin level and medical condition of the patients. There was highly statistical significance in digoxin level without ultrafiltration and with ultrafiltraton in the following medical condition: congestive heart failure with myopthy and congenital heart disease with heart failure. In heart failure with liver cirrhosis and healthy presons there was less statistical significance.

Table (8) shows relation between cardiac signs and digoxin level in the patients. There is highly statistical significance between digoxin level with and without ultrafiltration in patients with tachycardia (P<0.001) and less statistical significance in patients with bradycardia (P= 0.006).

Table (9) shows statistical data of digoxin level in the different cardiac manifestations.

Table (10) shows correlation between digoxin level and other manifestations like visual and gastrointestinal manifestations. There is no statistical significance between digoxin level and these manifestations.

DISCUSSION

Digoxin is a cardiac glycoside used most frequently to increase the adequacy of circulation in patients with congestive heart failure and to slow the ventricular rate in the presence of atrial fibrillation and flutter by blocking the atrioventricular node (Amitava, 2002).

The clinical side effects associated with high concentrations of digoxin in serum resemble the clinical condition for which the drug is administered (McEroy et al., 1997). So monitoring of serum digoxin concentrations is recommended and it is also important in cases of digoxin intoxication to determine the dose of antidote , in patients with descreased renal function to adjust digoxin dosage and in cases of concomitant intake of other drugs known to interact with digoxin pharmacokinetics e.g. quinidine (Roland et al., 1998).

Endogenous digoxin-like immunoreactive factors (DLIFs)present in mammalian blood were discovered in part as a consequence of their cross - reactivity with antidigoxin antibodies (Hassan et al., 1996). These factors may potentially interfere with digoxin immunoassay. They falsely elevate or lower measured serum digoxin concentration (Papradip and Amitava, 2004).

This study was done on fourty five blood samples taken from patients either on digoxin therapy, accidental or suicidal intake of digoxin to estimate the digoxin level in these patients aiming to adjust dose during digoxin therapy either in subtherapeutic or overdosed patients, or to treat patients of digoxin intoxication.

Evaluation of discrepancies between estimated, actual digoxin level and the clinical picture of the patients was done. Digoxin levels were estimated by TDx analyzer in Poison Laboratory at Emergency Hospital, Mansoura University.

The digoxin level without ultrafiltration has ranged from 4.36 ng/ml to 12.34 ng/ml with mean 7.48 $\pm$ 1.86. These levels didn't correlate with the clinical picture of the patients especially cardiac signs, the level has ranged from 5.43 to 6.70 ng/ml in patients with no cardiac manifestations. This ensures that the level didn't coincide with the clinical picture. This level decreased after ultrafiltration and ranged from 1.74 to 2.33 ng/ml; this range is within normal therapeutic range and is coincided with the clinical picture of the patients. There was significant difference between groups with Anova test ($P = 0.01$).

The digoxin level was remeasured after ultrafiltration. The level has ranged from 1.30 to 10.44 ng/m respectively with mean 5.63 $\pm$ 2.06.

The digoxin level with ultrafiltration was lower than the level without ultrafiltration in patients totally. This was significant between groups with Anova test ($P = 0.005$). It was significant with one paired t-test in patients with cardiomyopathy ($P < 0.001$), patients with heart failure and liver cirrhosis ($P = 0.026$), patients with heart failure and congenital heart disease ($P < 0.001$).

These results are attributed to the presence of endogenous digoxin - like immunoreactive factor (DLIFs) in the plasma of some patients. Our results are coincided with that of Hayashi et al., (2000) who found increased DLIFs in the plasma and cardiocytes of patients with hypertrophic cardiomyopathy. These DLIFs crossreact with antidigoxin antibody and falsely elevate immunoassay results. Amitava et al., (2005) found also the interference effect of these factors during measuring digoxin level by fluorescence polarization immunoassay (FPIA) in patients with liver disease and neonates. Ijiri et al., (2004) detected plasma DLIFs using FPIA in neonates with jaundice and without jaundice, and the least in healthy volunteers.

These findings are closely related to our findings which showed highly statistical significance ($P < 0.001$) between digoxin level without and with ultrafiltration in cases of congenital heart disease with failure of which five patients were neonates.

In healthy persons, the digoxin level didn't differ significantly before and after ultrafiltration. This may be attributed to the high serum level due to suicidal intake of digoxin, the low level of DLIFs and consequently the less interference in digoxin immunoassay. These results agree with the findings of Miller et al., (1996) who reported that the higher the digoxin concentration, the lower the interference by DLIFs. In other words, some samples with sufficient DLIF present to cause a discrepancy by itself may be nondiscrepant if the digoxin concentration is relatively high.

Also, our results coincide with that of Ijiri et al., (2004) who detected that the least DLIFs level was present in healthy volunteers.

In contrast to our results of positive interference observed in some of the assays, Steimer et al., (2002) showed false negative interference of digoxin assays by spironolactone and canrenone which are used in treatment of patients with servere heart failure.

Toxic concentrations resulting from positive interference alert both pathologists and clinicians and lead to further investigation, during which interference should be detected.

Negative interference of DLIFs in the digoxin assay may be problematic because

the clinician may increase the digoxin dose based on falsely low serum digoxin concentrations.

However, comparison of free and total digoxin concentrations can indicate the extent of DLIFs interference in immunoassays and considering the clinical picture of the patients may prove to be clinically more useful.

In conclusion, monitoring of free digoxin concentrations may be recommended if a clinician has questions about a digoxin level in some medical conditions like congenital heart disease, neonates, cardiomyopthy, liver cirrhosis, diabetes and renal failure, and confirmation of the results by high performance liquid chromatography is required in these conditions.

Table (1) : Statistical data of age, clinical and laboratory details of patients presented to Poison Unit at Emergency Hospital, Mansoura University.

	Mean ± SD	*Range*	*Anova test P*
Age			
★ Congestive HF+ myopathy	60.90±20.61	31.00- 90.00	
★ Healthy	22.27±13.69	0.50-55.0	
★ Diabetes	68.00±4.24	65.00-71.0	
★ Congestive HF(n:1)	71.00	71.00-71.0	
★ Chronic renal failure(n:1)	54.00	54.00-54.0	
★ Hf+ liver cirrhosis	54.00±4.24	51.0-57.0	
★ Congenital heart disease +HF	0.59±0.54	0.10-1.60	
★ Total	32.61±27.42	0.10-90.0	
Bilirubin			
★ Congestive HF+ myopathy	2.30±1.68	0.90-6.20	
★ Healthy	0.47±0.17	0.30-0.90	
★ Diabetes	2.30±0.28	2.10-2.50	
★ Congestive HF(n:1)	3.40	3.40-3.40	
★ Chronic renal failure(n:1)	1.50	1.50-1.50	< 0.001***
★ HF+ liver cirrhosis	4.20±1.41	3.20-5.20	
★ Congenital heart disease +HF	0.72±0.28	0.40-1.20	
★ Total	1.30±1.36	0.30-6.20	
Creatinine			
★ Congestive HF+ myopathy	2.37±1.11	090-4.10	
★ Healthy	0.73±0.38	0.30-1.80	
★ Diabetes	1.95±0.49	1.60-2.30	
★ Congestive HF+	2.90±	2.90-2.90	
★ Chronic renal failure	5.50±	5.50-5.50	
★ HF+ liver cirrhosis	1.50±0.56	1.10-1.90	
★ Congenital heart disease +HF	0.64±0.150	0.40-0.80	
★ Total	1.36±1.16	0.30-5.50	

***Highly significant

Table (2): Statistical data of sex in different medical conditions of patients presented to Poison Unit at Emergency Hospital, Mansoura University.

Medical conditions	*Sex*		*Total*	*Chi-square P*
	Male	*Female*		
Congestive HF +myopathy				
★ n	9	2	11	
★ %within medical conditions	81.8	18.2	100.0	
★ % of total	20.0	4.4	24.4	
Healthy				
★ n	10	9	19	
★ %within medical conditions	52.6	47.4	100.0	
★ % of total	22.2	20.0	42.2	
Diabetes				
★ n	2	-	2	
★ %within medical conditions	100.0	-	100	
★ % of total	4.4	-	4.4	
Congestive HF				
★ n	1	-	1	
★ %within medical conditions	100.0	-	100.0	
★ % of total	2.2	-	2.2	0.388
Chronic renal failure				
★ n	1	-	1	
★ %within medical conditions	100.0	-	100.0	
★ % of total	2.2	-	2.2	
HF+ liver cirrhosis				
★ n	2	-	2	
★ %within medical conditions	100.0	-	100.0	
★ % of total	4.4	-	4.4	
Congenital heart disease +HF				
★ n	5	4	9	
★ %within medical conditions	55.6	44.4	100.0	
★ % of total	11.1	8.9	20.0	
Total				
★ n	30	15	45	
★ % of total	66.7	33.3	100.0	

Table (3): Mode of digoxin intake in patients presented to Poison Unit at Emergency Hospital, Mansoura University.

Medical conditions	*Mode of intake*			*Total*	*Chi-squar P*
	Therapeutic	*Suicidal*	*Accidental*		
Congestive HF + myopathy					
★ n	9	2	-	11	
★ % of medical condition	81.8	18.2	-	100.0	
★ % of total	20.0	4.4	-	24.2	
Healthy					
★ n	-	17	2	19	
★ % of medical condition	-	89.5	10.5	100.0	
★ % of total	-	37.8	4.4	42.2	
Diabetes					
★ n	2	-	-	2	
★ % of medical condition	100.0	-	-	100.0	
★ % of total	4.4	-	-	4.4	
Congestive HF					
★ n	1	-	-	1	
★ % of medical condition	100.0	-	-	100.0	
★ % of total	2.2	-	-	2.2	<0.001***
Chronic renal failure					
★ n	1	-	-	1	
★ % of medical condition	100.0	-	-	100.0	
★ % of total	2.2	-	-	2.2	
HF+ liver cirrhosis					
★ n	2	-	-	2	
★ % of medical condition	100.0	-	-	100.0	
★ % of total	4.4	-	-	4.4	
Congenital heartdisease+HF					
★ n	9	-	-	9	
★ % of medical condition	100.0	-	-	100.0	
★ % of total	20.0	-	-	20.0	
Total					
★ n	24	19	2	45	
★ % of total	53.3	42.2	4.4	100.0	

*** Highly significant

Table (4): Cardiac manifestations of the patients presented to Poison Unit at Emergency Hospital, Mansoura University.

Medical condition	*Cardiac manifestations*			*Total*	*Chi-square P*
	Tachycardia	*Bradycardia*	*No cardiac manifestations*		
Congestive HF + myopathy					
★ n	10	1	-	11	
★ %within medical condition	90.90%	9.1%	-	100.0 %	
★ % of total	22.2%	2.2%	-	24.4%	
Healthy					
★ n	2	16	1	19	
★ %within medical condition	10.5%	84.2%	5.3%	100.0 %	
★ % of total	4.4%	35.6%	2.2%	42.2%	
Diabetes					
★ n	2	-	-	2	
★ %within medical condition	100. %	-	-	100.0 %	
★ % of total	4.4%	-	-	4.4%	
Congestive HF					
★ n	1	-	-	1	
★ %within medical condition	100.0%	-	-	100.0 %	
★ % of total	2.2%	-	-	2.2%	< 0.001***
Chronic renal failure					
★ n	-	-	1	1	
★ %within medical condition	-	-	100.0%	100.0 %	
★ % of total	-	-	2.2%	2.2%	
HF+ liver cirrhosis					
★ n	2	-	-	2	
★ %within medical	100.0%	-	-	100.0 %	
★ % of total	4.4%	-	-	4.4%	
Congenital heart disease +HF					
★ n	6	3	-	9	
★ %within medical condition	66.7%	33.3%	-	100.0 %	
★ % of total	13.3%	6.7%	-	20.0%	
Total					
★ n	23	20	2	45	
★ % of total	51.1%	44.4%	4.4%	100.0 %	

*** Highly significant (P<0.001)

Table (5): Visual and gastrointestinal (GIT) manifestations of the patients presented to Poison Unit at Emergency Hospital, Mansoura University.

Medical condition	*Visual manifestations*		*(GIT) manifestations*		*Total*
	+ve	*-ve*	*+ve*	*-ve*	
Congestive HF + myopathy					
★ n.	8	3	10	1	11
★ %within medical condition	72.7%	27.3%	90.90%	9.1%	100.0%
★ % of total	17.8%	6.7%	22.2%	2.2%	24.4%
Healthy					
★ n.	13	6	17	2	19
★ %within medical condition	68.4%	31.6%	89.5%	10.5%	100.0%
★ % of total	28.9%	13.3%%	37.8	4.4%	42.2%
Diabetes					
★ n.	2	-	1	1	2
★ %within medical condition	100.0%	-	50.0%	50.0%	100.0%
★ % of total	4.4%	-	2.2	2.2%	4.4%
Congestive HF					
★ N.	-	1	1	-	1
★ %within medical condition	-	100.0%	100.0%	-	100.0%
★ % of total	-	2.2%	2.2%	-	2.2%
Chronic renal failure					
★ n.	1	-	1	-	1
★ %within medical condition	100.0%	-	100.0%	-	100.0%
★ % of total	2.2%	-	2.2%	-	2.2%
HF+ liver cirrhosis					
★ n.	2	-	2	-	2
★ %within medical	100.0%	-	100.0	-	100.0%
★ % of total	4.4%	-	4.4%	-	4.4%
Congenital heart disease +HF					
★ n.	2	7	5	4	9
★ %within medical condition	22.2	77.8%	55.6%	44.4%	100.0%
★ % of total	4.4%	15.6%	11.1%	8.9%	20.0%
Total					
★ n.	28	17	37	8	45
★ % of total	62.2%	37.8	82.2%	17.8%	100.0%

Table (6): Statistical data of digoxin level in the different medical conditions of the patients presented to Poison Unit at Emergency Hospital, Mansoura University.

Digoxin level	*Mean ± SD*	*Range*	*Anova test P*
Digoxin level without ultrafiltration			
★ Congestive HF+ myopathy	8.93±2.27	4.50-12.34	
★ Healthy	6.97±1.21	4.36-9.54	
★ Diabetes	6.80±0.98	6.10-7.50	
★ Congestive HF(n:1)	6.85	6.85-6.85	0.114
★ Chronic renal failure (n:1)	5.43	5.43-5.43	
★ HF + liver cirrhosis	7.82±0.86	7.21-8.43	
★ Congenital heart disease +HF	7.18±2.17	5.17-11.20	
★ Total	7.48±1.86	4.36-12.34	
Digoxin level with ultrafiltration			
★ Congestive HF + myopathy	6.64±2.27	1.30-10.44	
★ Healthy	6.70±1.16	4.21-8.99	
★ Diabetes	4.36±0.36	4.11-4.62	
★ Congestive HF(n:1)	4.03	4.03-4.03	0.005*
★ Chronic renal failure(n:1)	2.33	2.33-2.33	
★ HF+ liver cirrhosis	5.63±0.98	4.93-6.33	
★ Congenital heart disease +HF	4.001±2.04	2.03-7.12	
★ Total	5.64±2.06	1.30-10.44	

*P is significant < 0.05

Table (7): Relation between digoxin level and medical condition of the patients presented to Poison Unit at Emergency Hospital, Mansoura University.

	Mean ±SD	*t-test* *P*
Congestive HF with myopathy		
★ digoxin level without ultrafiltration	8.93±2.27	< 0.001***
★ digoxin level with ultrafiltration	6.64±2.27	
Healthy		
★ digoxin level without ultrafiltration	6.97±1.21	0.001
★ digoxin level with ultrafiltration	6.70±1.16	
Diabetes		
★ digoxin level without ultrafiltration	6.80±0.98	0.235
★ digoxin level with ultrafiltration	5.36±1.77	
Congestive HF*		
★ digoxin level without ultrafiltration	6.85	—
★ digoxin level with ultrafiltration	4.03	
Chronic renal failure*		
★ digoxin level without ultrafiltration	5.43	—
★ digoxin level with ultrafiltration	2.33	
HF+ liver cirrhosis		
★ digoxin level without ultrafiltration	7.82±0.86	0.026
★ digoxin level with ultrafiltration	5.63±0.98	
Congenital heart disease+HF		
★ digoxin level without ultrafiltration	7.18±2.17	<0.001***
★ digoxin level with ultrafiltration	4.00±2.04	

* The correlation and t-test can not be computed because the sum of caseweights is less than or equal to 1.

*** Highly significant.

Table (8): Relation between cardiac signs and digoxin level in the patients presented to Poison Unit at Emergency Hospital, Mansoura University.

	Mean ±SD	*t-test* *P*
Tachycardia		
★ digoxin level without ultrafiltration	7.74±1.95	<0.001***
★ digoxin level with ultrafiltration	5.48±2.23	
Bradycardia		
★ digoxin level without ultrafiltration	7.34±1.80	0.006
★ digoxin level with ultrafiltration	6.47±1.57	
No caradiac manifestations		
★ digoxin level without ultrafiltration	6.06±0.89	0.508
★ digoxin level with ultrafiltration	4.53±3.11	

*** Highly significant

Table (9): Statistical data of digoxin level in the different cardiac manifestations in the patients presented to Poison Unit at Emergency Hospital, Mansoura University.

	Mean ±SD	Range	*Anova test P*
Digoxin level without ultrafiltration			
★ Tachycardia	7.74±1.95	4.50-12.34	0.434
★ Bradycardia	7.34±1.80	4.36-11.20	
★ No cardiac manifestations	6.06±0.89	5.43-6.70	
★ Total	7.48±1.86	4.36-12.34	
Digoxin level with ultrafiltration			
★ Tachycardia	5.48±2.23	1.30-10.44	0.010*
★ Bradycardia	6.47±1.57	2.11-8.99	
★ No cardiac manifestations	4.53±3.11	1.74-2.33	
★ Total	5.64±2.06	1.30-10-44	

* P is significant if <0.05

Table (10): Correlation between digoxin level and visual&GIT manifestations in the patients presented to Poison Unit at Emergency Hospital, Mansoura University.

	digoxin level without ultrafiltration	digoxin level with ultrafiltration
Visual		
★ Pearson correlation	0.033	0.054
★ Significance	0.865	0.782
GIT		
★ Pearson correlation	0.069	0.145
★ Significance	0.682	0.386
Digoxin level without ultrafiltration		
★ Pearson correlation	1.00	0.716*
★ Significance	-	0.00
Digoxin level with ultrafiltration		
★ Pearson correlation	0.716*	1.00
★ Significance	0.00	-

*Correlation is significant at the 0.01 level (2-tailed).

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المتناقضات فى الكشف عن الديجوكسين بتحليل المناعة الإنزيمية الفلوريسينية

المشتركون فى البحث

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يعتبر الديجوكسين من أكثر أدوية القلب إستخداماً، ولقد قيد إستعماله بتراوح تركيزه العلاجى من ٨ر٠ إلى ٢ نانوجرام / المللى فى مصل الدم إلى ٥ر٢ نانوجرام / المللى، وقد أنقصت مراقبة تركيز الدواء العلاجى نسبة حدوث التسمم المتعمد أو العرضى.

وأجريت هذه الدراسة على ٤٥ عينة دم من مرضى تتراوح أعمارهم من شهر إلى ٩٠ عام، وهم ذوى حالات صحية مختلفة (١١ مريض بإعتلال فى عضلة القلب مع هبوط القلب، ١٩ شخص لايعانون من أية أمراض، مريضين بداء البول السكرى، مريض بهبوط القلب الاحتقانى، مريض بالفشل الكلوى، مريضين بالتليف الكبدى مع هبوط القلب، تسعة مرضى بالأمراض القلبية الخلقية)، وذلك لتقييم المتناقضات بين مستوى الديجوكسين المقاس الكلى (المرتبط بالبروتينات) والحقيقى (الحُر) والحالة الإكلينيكية للمرضى.

وقد تم تحليل مستوى الديجوكسين بجهاز المناعة الإنزيمى حيث تم قياسه بدون ترشيح ثم بعد ترشيح العينات بواسطة فلاتر خاصة تقوم بحجز البروتينات التى تتداخل مع التحليل، ولقد لوحظ أن مستوى الديجوكسين بعد الترشيح كان أقل من مستواه بدون ترشيح فى المرضى عموماً، ووجدت دلالة إحصائية بين المجموعات، وكان له دلالة إحصائية عالية فى مرضى إعتلال عضلة القلب، وحالات أمراض القلب الخلقية مع هبوط القلب، وأقل دلالة إحصائية كانت فى مرضى التليف الكبدى مع هبوط القلب.

ووجدت أيضاً دلالة إحصائية بين مستويات الديجوكسين فى المرضى الذين يعانون من زيادة أو بطء فى ضربات القلب، ولم توجد دلالة إحصائية فى الأعراض الأخرى مثل الأعراض البصرية والمعدى معوية.

ولهذا يجب أن تفسر نتائج قياسات مستوى الديجوكسين بتحليل المناعة الإنزيمية بدقة فى بعض الحالات المرضية مثل أعراض القلب الخلقية، إعتلال عضلة القلب، تليف الكبد، وحديثى الولادة، ويعاد قياس العقار بعد ترشيح العينات خاصة إذا لم تتفق الحالة الإكلينيكية مع مستوى العقار فى الدم، ويجب أن يقاس مستوى الديجوكسين بجهاز الكروماتوجراف السائل عالى الكفاءة خاصة فى حالات وجود أعراض قلبية فى الحالات المرضية السابقة، وأيضاً فى حالات التسمم بالديجوكسين لحساب جرعة الترياق المضاد بدقة.