Turkish Journal of Emergency Medicine 16 (2016) 17–21

Contents lists available at ScienceDirect

Turkish Journal of Emergency Medicine

journal homepage: http://www.elsevier.com/locate/TJEM

Original article

Retrospective evaluation of patients with elevated digoxin levels at an emergency department

Gulsum Limon [a], Gurkan Ersoy [b], Nese Colak Oray [b], Basak Bayram [b], Onder Limon [c, *]

[a] Izmir University School of Health Sciences, First Aid and Emergency Care Program, Izmir, Turkey
[b] Dokuz Eylul University, Faculty of Medicine, Department of Emergency Medicine, Izmir, Turkey
[c] Izmir University, Faculty of Medicine, Department of Emergency Medicine, Izmir, Turkey

ARTICLE INFO

Article history:
Received 21 August 2015
Received in revised form
5 October 2015
Accepted 14 October 2015
Available online 14 March 2016

Keywords:
Digoxin
Digoxin level
Intoxication
Emergency department

ABSTRACT

Objectives: We investigated the demographic characteristics, clinical and laboratory findings, treatment strategies and clinical outcomes of patients presenting at emergency department (ED) with digoxin levels at or above 1.2 ng/ml.

Materials and methods: The demographic and clinical characteristics of patients with serum digoxin levels at or above 1.2 ng/ml admitted to an ED between January 2010 and July 2011 were investigated in this cross-sectional descriptive study. Patients with ECG and clinical findings consistent with digoxin toxicity and no additional explanation of their symptoms were evaluated for digoxin toxicity.

Results: In this study 137 patients were included, and 68.6% of patients were women with mean age 76.1 ± 12.2. There was no significant difference between gender and digoxin intoxication. The mean age of intoxicated group was significantly higher than the non-intoxicated group (P = 0.03). The most common comorbidities were congestive heart failure (n = 91) and atrial fibrillation (n = 74). The most common symptoms were nausea, vomiting and abdominal pain. The levels of hospitalization and mortality in this group were significantly higher.

Conclusion: Digoxin intoxication must be suspected in patients present in the ED, particularly those with complaints that include nausea and vomiting, as well as new ECG changes; serum digoxin levels must be determined.

1. Introduction

Despite the introduction of new drug classes for managing congestive heart failure (CHF) and atrial fibrillation (AF), many patients admitted to emergency departments (EDs) continue to be managed with cardiac glycosides. Cardiotoxicity from cardiac glycosides may present obvious symptoms, such as nausea, vomiting, and hypotension, or may be more subtle with nonspecific symptoms.[1] The difficulty in diagnosing patients with digitalis intoxication can be attributed to several factors: 1) the signs, symptoms and electrocardiogram (ECG) manifestations can be attributed to the underlying disease process for which the drug is prescribed; 2) the narrow therapeutic window of digoxin, which causes great variability in the sensitivity of individuals toward the drug; 3) the lack of any dysrhythmia diagnostic of toxicity.[2,3] Chronic toxicity occurs in 4–10% of the patients taking digitalis but is suspected in only 0.25% of all cases[4,5]

Few studies have probed the incidence of toxicity and the factors that affect the toxicity observed among patients presenting to ED, despite the clinical importance of digoxin toxicity. We enacted this cross-sectional retrospective study to investigate the demographic characteristics, clinical and laboratory findings, treatment strategies and clinical outcome of patients presenting at our ED whose digoxin levels were 1.2 ng/ml or above. The threshold 1.2 ng/ml is adopted because of the reported increased mortality above 1.2 ng/ml in the study of Rathore et al.[6]

2. Materials and methods

This cross-sectional, descriptive review included the cases with digoxin levels at or above 1.2 ng/ml at an ED between January 2010

* Corresponding author. Tel.: +90 0505 525 26 52, 905055252652 (mobile).
E-mail address: dronderlimon@yahoo.com (O. Limon).

Peer review under responsibility of The Emergency Medicine Association of Turkey.

http://dx.doi.org/10.1016/j.tjem.2015.10.001

and July 2011. The study population was selected from the hospital information system according to their digoxin levels regardless of the presenting clinical symptoms or findings. Patients with missing data were excluded from the study.

The study protocol was approved by the ethics committee and was conducted in accordance with the Declaration of Helsinki.

The day of admittance (day/month/year), as well as the ages, genders, states of acute or chronic drug intake, comorbidities, clinical findings, test results (ECG, as well as laboratory findings for glucose, blood urea nitrogen, creatinine, sodium, potassium, chlorine, complete blood count, CK-MB, troponin), treatment information, blood digoxin levels and clinical outcomes, of the patients were recorded using standard data forms.

Patients with ECG and clinical findings consistent with digoxin toxicity and for whom there was no additional explanation of symptoms were evaluated as suffering from digoxin toxicity. Digoxin toxicity was studied based on acute or chronic usage, as listed below.

Acute toxicity is indicated by the following:

1. The presence of dysrhythmias, dysrhythmias with decreased AV conduction or/and increased automaticity (e.g., AF with AV block, accelerated junctional rhythm), premature ventricular contractions (PVCs) (particularly bigeminy or trigeminy) or supraventricular tachyarrhythmias with rapid ventricular rates.[7]
2. Hyperkalemia (≥5.5 mEq/L).[8]
3. Probable clinical findings other than cardiac findings.[3]

Chronic toxicity is indicated by the following:

1. Bradyarrhythmias (may be ventricular tachyarrhythmias)
2. Normal to low serum potassium levels (may be high)[8]
3. Increased serum digoxin levels (expected therapeutic level <1.2 ng/ml)[6]
4. Probable clinical findings other than the cardiac findings include the following;
   a. Weakness
   b. Gastrointestinal system: anorexia, nausea, vomiting or abdominal pain
   c. Central nervous system: headache, thoughtfulness, hallucinations, delirium or photophobia, visual disturbances (yellow-green dyschromatopsia)[3]

2.1. Statistical analysis

The data recorded in Statistical Package for the Social Sciences (SPSS) 16 for Windows statistical software (SPSS Inc., Chicago, IL, USA). The qualitative variables are expressed as a % and the estimation of 95% confidence interval (CI). The quantitative variables are expressed as the mean ± S.D. The means were compared using Student's t-test or the Mann–Whitney U-test as applicable after verifying normality using the Kolmogorov–Smirnov test. The association of qualitative variables was made using the Chi-square test. Test results with p values <0.05 were determined to be statistically significant.

3. Results

During the study period, 124.557 patients arrived at the ED; 139 patients had digoxin levels 1.2 ng/ml or higher. Two of the patients were excluded from the study due to a lack of data, and 137 patients were included. The patients included in the study accounted for 0.11% of the patients who arrived at the ED during the study period (Fig. 1).

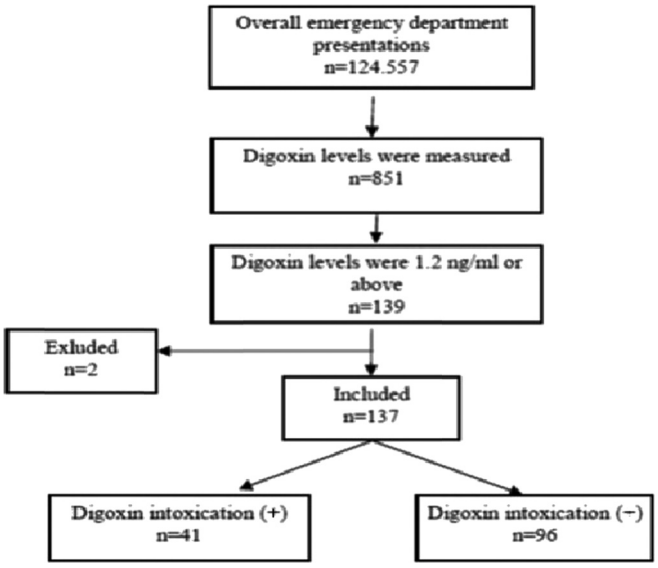

Fig. 1. Algorithm for the study population.

Among the patients included in the study, 43 (31.4%) were male, and 94 (68.6%) were female; the mean age was 76.1 ± 12.2. The youngest patient was 20, and the oldest patient was 104 years old. Two (1.5%) patients arrived after acute oral intake, one patient (0.7%) had with acute exposure during chronic intake and 134 (97.8%) patients were chronic users. The mean ages of the patients with acute and chronic intake were 57.5 ± 50.2 and 76.3 ± 11.3, respectively. There was no significant difference between the age groups ($P > 0.05$). Digoxin was the only drug taken by 135 (98.5%) of the patients. The exposures occurred with oral intake.

When evaluated using the clinical, laboratory and ECG findings, 29.9% (n = 41) of patients were considered to have digoxin toxicity, and 70.1% (n = 96) of the patients only had high blood digoxin levels but were not intoxicated. In the intoxicated group, one patient presented with acute toxicity, and 39 presented with chronic toxicity. There was no significant difference between the intoxicated and non-intoxicated groups in the context of gender ($P > 0.05$). The mean age of intoxicated group was significantly higher than that of the non-intoxicated group (79.8 ± 11.8 and 74.6 ± 12.1, respectively, $P = 0.03$). No significant differences were found between the comorbid diseases of the patients and digoxin toxicity (Table 1).

We found that the most common final diagnoses other than digoxin intoxication were CHF (n = 24, 17.5%) and acute renal failure (n = 13, 9.4%). Sixteen (11.6%) patients had more than one diagnosis (Table 2).

The potassium level is significantly higher in the intoxicated group when the biochemical markers are evaluated (Table 3).

Table 1
The relationship between elevated digoxin levels and comorbid diseases.

Comorbid disease	Digoxin toxicity				p	X^2
	Yes	%	No	%		
CHF	27	65.9	64	66.7	>0.05	0.03
AF	26	63.4	48	50	>0.05	2.75
HT	23	56.1	48	50	>0.05	0.73
CAD	13	31.7	27	28.1	>0.05	0.29
Other	10	24.4	37	37.5	>0.05	2.17
DM	9	21.9	22	22.9	>0.05	0.01
Cardiac valve disease	4	0.9	14	14.6	>0.05	0.49