Original Article

Impact of Digoxin on Over All Mortality in Patients with Heart Failure and Atrial Fibrillation

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ABSTRACT

Objective: The practice of digoxin in patients having a trial fibrillation (AF) with heart failure and deprived of heart failure has not been discussed. The purpose of this analysis was to investigate the effect of digoxin therapy on frequency of mortality stratified by heart failure.

Study Design: prospective / observational study

Place and Duration of Study: This study was conducted at the Chaudhary Pervaiz Elahi Institute of Cardiology, Multan, Pakistan. Patients included from January 2020 to January 2021 and were enrolled for a year.

Materials and Methods: This study encompassed 610 patients of atrial fibrillation. The analyzes were achieved using multivariate and univariate statistics.

Results: The study included 610 patients. 46 + 11 years was the patients mean age. At discharge from hospital, 34% (n = 214) of patients were prescribed digoxin and among 48% (n = 103) have heart failure. Discharged 75 (12.3%) patients died after 1year of follow-up. Patients with heart failure had higher mortality at one month (4.2% vs 2.0% without HF; p <0.001), at 6 months (12.1% vs 4.3 without HF%; p <0.001) and at 12 months (23.4% vs 6.9 without HF%; p <0.001).When stratified digoxin therapy showed significantly higher mortality at one-year in patients with heart failure (at 12-month (24.1% vs 11.1% without HF and at 6-months 11.1% vs 7.9% without HF).

Conclusion: In heart failure and atrial fibrillation patients, survival did not improve by digoxin. Though, in subjects deprived of heart failure, treatment with digoxin was related with significantly long-standing mortality.

Key Words: digoxin, atrial fibrillation, heart failure and mortality

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INTRODUCTION

With the development of approved drugs and more operative intervention procedures for the treatment of heart failure and a trial fibrillation (AF), the digoxin usage has decreased for the past two eras[1-2]. In the American Heart Association /Heart Rhythm Society/ American College of Cardiology (AHA /HRS/ ACC) strategies for controlling the incidence of a trial fibrillation, digoxin, though cited in the treatment but does not provide class recommendations, otherwise recommends digoxin for HF pre-excitation, heart rhythm (class IB) and digoxin is operative in controlling the inactive rate of heart in subjects with reduced EF having HF (class IC)[3-4]. In addition, combinations of digoxin and B blockers (or in patients with heart failure fixed by a non-dihydropyridine calcium channel blocker) make sense in the monitoring and use of patients with AF (Class IIA)[5-6]. European Society of a trial Fibrillation (ESC) guidelines recommend the use of digoxin after beta-blockers and calcium channel blockers as a third option in patients with idiopathic or associated a trial fibrillation (class IB) and heart failure, guidelines of ESC indorse IV class IB digoxin) and for frequency control in long-lasting conditions, digoxin in heart failure are recommended in subjects with sedentary lifestyle and left ventricular (LV) dysfunction[7-8]. Though, in practice, digoxin has remained to be overused or misused in AF patients, particularly in the aged populace and causes noxiousness[9]. Recent reports of the use of digoxin have raised controversy regarding the mortality and morbidity of patients with or without heart failure[10-11]. Due to the safety concerns of digoxin and recent reports, more evidence is needed before the digoxin policy can be changed. The purpose of this analysis was to investigate the effect of digoxin therapy on frequency of mortality graded by heart failure.

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MATERIALS AND METHODS

This is a prospective, and observational study which encompassed 610 patients of a trial fibrillation. Patients included from January 2020 to January 2021 and were enrolled for a year held in the Cardiology Department of Chaudhary Pervaiz Elahi Institute of Cardiology, Multan, Pakistan. All the particulars of the definitions and methods of data variables are available already. In summary, when patients were above 18 years of age, if they were entitled to have AF either on a 12-lead ECG electrocardiogram for 30 seconds time or having rhythm strip were included and received written permission. The treatment choices are according to the doctor of medicine. The research was approved by the ethical committee. The data was documented in a standard case description form and uploaded online. Data gathered comprised selectees' demographics; surgical and medical history; AF History, including AF-type; in emergency outcomes and management given at before, at discharge and during stay in hospital. Medications include diuretics, converting enzyme (ACEI) inhibitors, angiotensin, angiotensin receptor blockers, B blockers, statins, clopidogrel, warfarin and aspirin. Data complies with the AHA/ ACC guidelines for AF. Variables necessary for Hypertension, congestive heart failure, Age above 75 years; DM; the transient ischemic attack/ stroke was also calculated. HF was definite rendering to the criteria of Framingham listed in the AHA/ ACC variables data. LV systolic dysfunction was definite after EF less than 40% determined by ECHO.

The characteristics of patient were concise using categorical variables and mean rates, standard deviations and percentages between cases of continuous variables were measured and applied. The comparisons of groups of categorical variables were made using the Pearson's w2 test, followed by the Wilcoxon-man-Whitney test or Student's t-test, respectively. The effect of treatment by digoxin on overall mortality (30 days, 180 days and one year) was assessed by multivariate logistic regression using a step-by-step elimination approach. The mortality variables were as follows (Table 1) ($p < 0.1$). Changes include gender, age, LV systolic dysfunction, body mass index (BMI), diabetes, hypertension, chronic obstructive pulmonary disease (BPK), coronary artery disease (CAD),previous history of stroke / TIA, serum creatinine and peripheral vascular disease (PVD) were documented. The drugs prescribed in discharge include (diuretic, statin, beta-blocker, aspirin, warfarin, clopidogrel), type of AF and CHADS risk assessment were also recorded. The adaptive advantage of the logistics model was analyzed using Leme showand Hosmer statistical adapters. The discriminant potential of the logistic model was evaluated in the areas below the receiver efficiency curve, also called the C index. P value less than 0.05 was taken significant. Statistical analysis was achieved by means of STATA version 13.1.

RESULTS

The study included 610 patients. The clinical characteristics and demographic of the patients are presented in Table 1. 46±11 years was the patients mean age.

At discharge from hospital, 34% (n = 214) of patients were prescribed digoxin and among48% (n = 103) have heart failure. Discharge 75 (12.3%) patients died after 1year of follow-up.

Patients with heart failure had higher mortality at one month (4.2% vs 2.0% without HF; $p < 0.001$), at 6 months (12.1% vs 4.3 without HF%; $p < 0.001$) and at 12 months (23.4% vs 6.9 without HF%; $p < 0.001$).When stratified digoxin therapy showed significantly higher mortality at one-year in patients with heart failure (at 12-month (24.1% vs 11.1% without HF and at 6-months 11.1% vs 7.9% without HF).

Table No.1: Clinical characteristics and demographic of the patients

Characteristic	All (N =610)	Digoxin Therapy at Discharge		P
		No (n=396; 65%)	Yes (n=214; 35%)	
Demographic				
Age, mean ±SD, years	46 ±11	47 ±10	46 ±12	0.638
Male gender, n (%)	321 (52.6%)	225 (56.8%)	96 (44.9%)	<.001
Medical history, n (%)				
LV systolic dysfunction	109 (17.9%)	42 (10.6%)	67 (31.3%)	<.001
Heart failure	168 (27.5%)	65 (16.4%)	103 (48.1%)	<.001
Coronary artery disease	178 (29.2%)	105 (26.5%)	73 (34.1%)	0.001
Diabetes mellitus	184 (30.2%)	125 (31.6%)	59 (27.6%)	0.051
Rheumatic heart disease	98 (16.1%)	28 (7.1%)	70 (32.7%)	<.001
Hypertension	316 (51.8%)	209 (52.8%)	107 (50.0%)	0.052
COPD	34 (5.6%)	18 (4.5%)	16 (7.5%)	0.035
Stroke/TIA	75 (12.3%)	47 (11.9%)	28 (13.1%)	0.016

Peripheral vascular disease	13 (2.1%)	6 (1.5%)	7 (3.38%)	0.001
Creatinine, median (interquartile range), mmol/L	82 (68-100)	70 (59-101)	76 (62-103)	<.001
BMI, mean + SD, kg/m^2	23 + 4	24 + 4	22 + 4	<.001
Smoking status	131 (21.5%)	82 (20.7%)	49 (22.9%)	0.54
CHADS score category, n (%)				
0	172 (28.2%)	121 (30.6%)	51 (23.8%)	<.001
1	164 (26.9%)	107 (27.0%)	57 (26.6%)	0.642
2-6	274 (44.9%)	168 (42.4%)	106 (49.5%)	<.001
AF type, n (%)				
Don't know	21 (3.4%)	14 (3.5%)	7 (3.3%)	0.778
Paroxysmal	114 (18.7%)	94 (23.7%)	20 (9.3%)	<.001
First attack ever	221 (36.2%)	169 (42.7%)	52 (24.3%)	<.001
Persistent	56 (9.2%)	35 (8.8%)	21 (9.8%)	0.52
Permanent	198 (32.5%)	84 (21.2%)	114 (53.3%)	<.001
Medications at discharge, n (%)				
ACEI	238 (39.0%)	144 (36.4%)	94 (43.9%)	0.002
Diuretic	333 (54.6%)	158 (39.9%)	175 (81.8%)	<.001
b-Blocker	346 (56.7%)	245 (61.9%)	101 (47.2%)	<.001
ARB	80 (13.1%)	56 (14.1%)	24 (11.2%)	0.083
Aspirin	323 (53.0%)	224 (56.6%)	99 (46.3%)	0.001
Statin	287 (47.0%)	206 (52.0%)	81 (37.9%)	<.001
Warfarin	351 (57.5%)	189 (47.7%)	162 (75.7%)	<.001
Amiodarone	57 (9.3%)	46 (11.6%)	11 (5.1%)	<.001
Clopidogrel	68 (11.1%)	51 (12.9%)	17 (7.9%)	0.037
Mortality, n (%)				
1 month	17 (2.8%)	9 (2.3%)	8 (3.7%)	0.084
6 months	50 (8.2%)	22 (5.6%)	28 (13.1%)	<.001
12 months	75 (12.3%)	35 (8.8%)	40 (18.7%)	<.001

Table No.2: Comparison of Mortality among the patients at various interval

Mortality Stratified by CHF Status	All	Pearson χ2 Test		P	Multivariate Logistic Regression			
		No Digoxin	Digoxin		OR (95% CI)	Adjusted P	HL	ROC
1 month								
Without HF	19 (2.0%)	10 (2.1%)	9 (2.9%)	0.561	1.15 (0.22-4.75)	0.742	0.101	0.67
With HF	16 (4.2%)	7 (3.9%)	11 (4.9%)	0.796	2.52 (0.61-9.57)	0.138	0.724	0.72
6 months								
Without HF	58 (4.3%)	27 (3.1%)	21 (7.9%)	<.001	4.97 (2.25-10.0)	<.001	0.895	0.73
With HF	77 (12.1%)	17 (13.5%)	50 (11.1%)	0.246	1.52 (0.70-3.19)	0.167	0.84	0.59
12 months								
Without HF	93 (6.9%)	50 (5.7%)	33 (11.1%)	<.001	4.12 (2.13-7.89)	<.001	0.061	0.71
With HF	112 (23.4%)	31 (21.5%)	71 (24.1%)	0.443	1.27 (0.73-2.43)	0.307	0.806	0.57

DISCUSSION

The main finding of this study was that in patients without HF and with AF, digoxin treatment was related with suggestively advanced long-term mortality equated to patients who did not receive digoxin treatment[10-11]. Moreover, in cases with HF and AF, digoxin did not show an endurance benefit. In a recent huge analysis of 132005 freshly detected AF patients with a mean age of 72.2 years, 22.9% had given digoxin[12-13]. In contrast, the mean age of patients with AF in this study was 46 ± 11%. In the analysis of stroke prevention with an oral thrombin inhibitor in a trial fibrillation [SPORTIF] III and V show promising effects, in patients with AF receiving digoxin, the mortality was 4.22% per patient-year compared with 2.66% per patient-years in those receiving digoxin were not observed with an adjusted hazard ratio (HR) of 1.53[14]. Similar HRe of 1.42 and 1.41 were observed in patients treated with digoxin in the Swedish Intensive Care Admission Information and Knowledge Registry (RIKS-HIA) observed in the AF Follow-up AFFIRM study. The causes of the increased death rate from digoxin in patients with HF and AF are unknown[15-16].

Digoxin has been associated with malignant tumors, prothrombotic status, markers of endothelial activation, stroke, increased mortality in patients with renal failure and digoxin-induced arrhythmiaswithoutHF[17-18]. Therefore, relatively healthy young patients who do not have AF have a high risk of death after one year after stopping digoxin treatment[19-20]. Inform health authorities about use of digoxin in AF patients in the Middle East. The main limitation of these studies is the observational design, which limits the ability to assess causation. The study could not confirm whether patients who are controlling or switching to other medications are taking digoxin. In addition, no digoxin doses and serum digoxin levels were available, making it difficult to determine whether digoxin levels may in any way contribute to mortality.

CONCLUSION

This is the initial study in the Pakistan. In subjects with a trial fibrillation deprived of heart failure, treatment with digoxin had a suggestively longer life span equated to those who did not receive treatment with digoxin. Moreover, in HF and AF patients, digoxin did not show endurance benefit. These conclusions must be taken seriously as the A trial fibrillation in the younger age. These results suggest that doctors must consider more medications before administering other medications to control the HR before prescribing digoxin in subjects with atrial fibrillation deprived of heart failure.

Author's Contribution:

Concept & Design of Study:	Khawar Abbas
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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