The European Research Journal 2019;5(3):461-466 ORIGINAL ARTICLE

Effect of low-dose dopamine on depression score in patients with heart failure

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DOI: 10.18621/eurj.376910

ABSTRACT

Objectives: This study aimed to assess the effects of low-dose dopamine on patients with depression in the intensive coronary unit.

Methods: Relatives of 43 ICU patients enrolled in the study. Sociodemographic characteristics of patients and their families recorded. Patients evaluated basal echocardiographic and biochemical values measured in the patient group. The Beck Anxiety and Depression Scale was used to assess anxiety and depression. The assessment performed by Beck scale at the 1st and 24th hour.

Results: The final study population consisted of 42 patients hospitalized with heart failure. Mean patient age was 67.5 ± 12.6 years. Average EF was 23.5% ± 8.7% and mean ProBNP was 6343.76 pg/mL in our study population. Changes of before and after dopamine treatment in depression score of heart failure patients was showed significantly (before value: 18.95 ± 9.89; after value: 17.29 ± 10.30, $p < 0.001$) however systolic and diastolic pressure difference was not significant.

Conclusion: Depression increased mortality and hospitalization in patients with heart failure. Therefore, it is an essential trial because of low-dose dopamine improve depression score in intensive care patients. However, prospective studies were needed to assess the long-term efficacy of dopamine.

Keywords: low dose dopamine, depression, Beck depression-anxiety scale, heart failure

Received: January 10, 2018; Accepted: June 1, 2018; Published Online: June 6, 2018

Symptoms of depression are common morbidity, affecting roughly 40% of patients with heart failure (HF) and are related to a reduced living standard [1-3]. Symptoms of depression have negative impacts not only on daily social and domestic activities but also on hospitalizations and mortality rates in HF patients [4]. Depressive symptoms contain depressed mood, guilt, hopelessness, low self-esteem, fatigue, sleep disturbances, appetite change, and inability to concentrate [5]. They measure by self-report instruments for these symptoms are subjective(for example Beck depression-anxiety scale) [6]. Previous studies have ensured evidence about the epidemiology factors, and results of depressive symptoms in patients with HF [5, 7]. However, our understanding of the patients with HF in the hospital and how to treat is not clear.

Dopamine and other inotropes have been in use for many years for the treatment of patients with acute decompensated systolic heart failure, known as heart failure with reduced left ventricular ejection fraction (HFrEF) too. Inotropic agents improve the contractility of the myocardium but can impress the peripheral vascular resistance and heart rate too.The

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e-ISSN: 2149-3189

most prevalent use of inotropes is amongst hospitalized patients with HFwith signs of end-organ dysfunction because of low cardiac output. Inotropic drugs can be used in patients with advanced systolic heart failure awaiting heart transplant to resume hemodynamic stability, or as a bridge to a decision. Dopamine is primarily an inotropic agent that has additive effect on renal blood flow(1 to 5 mcg/kg/min), additive effect on cardiac output and contractility(5 to 10 mcg/kg/min) and Alfa adrenergic effect(> 10 mcg/kg/min). This study aimed to determine the effect of renal dose dopamine on depression in HF patients using Beck Depression scale. We know that dysfunction of dopaminergic system is related to depression; however, dopamine cannot pass through the blood-brain barrier.

METHODS

Patients with a history of chronic HF-based on left ventricular systolic dysfunction with moderate to severe HF symptoms (class III or IV) included in the study. All patients were undergoing standard therapy for HF. Inclusion in the study required the simultaneous presence of the following criteria: Age > 18 years, history of HF, deterioration of HF symptoms of recent onset (< 6 hours), namely, dyspnea at rest, orthopnea, and paroxysmal nocturnal dyspnea, accompanied by signs of congestion (third heart sound, jugular venous distension, pulmonary rales) on physical examination, levels of serum B-type natriuretic peptide (BNP) > 400 pg/mL or N-terminal proBNP > 1,500 pg/ml .Patients excluded from the study if they had: Acute de novo HF, severe renal failure (admission serum creatinine > 215 mmol/L [2.5 mg/dL] or estimated GFR < 30 mL, 1.73 m2), admission systolic blood pressure < 90 mm Hg, severe valvular disease, known adverse reactions to furosemide or dopamine, HF secondary to congenital heart disease, a scheduled procedure with a need for IV contrast dye in the present hospitalization, a scheduled cardiac surgery within 2 months. The total number of patients was 50. However, 42 patients fulfilled all inclusion criteria and enrolled in the study. Before enrollment, each of the patients gave informed consent according to the local institutional ethical guidelines. On the patient's arrival at the emergency department, hemodynamic parameters (systemic systolic and diastolic blood pressure, heart rate, and

Table 1. Demographic characteristics of patients

Characteristics	HF patients (n=43)
Age (years)	67.5 ± 12.6
Sex (male)	34 (80%)
CAD	30 (70%)
DM	12 (28%)
HT	26 (60%)
HL	18 (42%)
EF (%)	23.5 ± 8.7
LVEDD (mm)	62.0 ± 6.2
LVESD (mm)	53.0 ± 9.9
LAA (cm²)	28.6±4.5
RAA (cm²)	27.9±2.9
Systolic/diastolic blood pressure (mmHg)	115/70
Total diuretic dose (mg)	151.43 ± 33.97

Data are presented as mean ± standard deviation or number (%) of the patient. CAD = coronary artery disease, DM = diabetes mellitus, HT = hypertension, EF = ejection fraction, LVEDD = left ventricle end-diastolic diameter, LVESD = left ventricle end systolic diameter, LAA = left atrial area, RAA = right atrial area, HF = heart failure

Table 2. Laboratory findings of patients

Parameters	Minimum	Maximum	Mean value	SD
Hb (g/dL)	8.20	14.80	12.5	1.55
BUN (mg/dL)	12.10	41.10	22.6	7.50331
Cr (mg/dL)	0.58	1.71	1.05	0.29383
Na (mEq/L)	128.00	143.00	137.71	3.67115
K (mEq/L)	3.50	5.19	4.33	0.45277
ProBNP (pg/mL)	908	21000	6343.76	5580.909
CRP (mg/dL)	0.01	5.09	1.10	1.10181
Uric acid (mg/dL)	4.00	9.90	6.61	1.74783
Ferritin (ng/mL)	11	179	69.33	46.156
Troponin I (ng/mL)	0.01	0.21	0.0233	0.04309

Hb = hemoglobin, BUN = blood urea nitrogen, Cr = creatinine, Na = sodium, K = potassium, CRP = C-reactive protein

respiratory rate) measured, intravenous access established, venous samples took for blood gas, electrolyte, and cardiac enzyme estimations and baseline clinical, echocardiographic parameters assessed. The initial therapeutic approach consisted of IV furosemide infusion for all patients and a continuous IV infusion of 3 mcg/kg/min dopamine.

Statistical Analysis

Continuous variables are expressed as mean ± 1 SD, and categoric variables are expressed as proportions. Study group characteristics compared with the Mann-Whitney test (continuous variables) and the Fisher exact test (categoric variables). Repeated values evaluated with the nonparametric Wilcoxon signed rank test. Statistical significance set at a P-value of < 0.05. All statistical analyses were performed using SPSS version 17.0 for Windows (SPSS, Chicago, IL).

RESULTS

The final study population consisted of 42 patients hospitalized with heart failure. We assessed patient characteristics. Mean patient age was 67.5 ± 12.6 years. The most common comorbidities included hypertension (n = 26), coronary atherosclerosis (n = 30), disorders of lipid metabolism (n = 18), and diabetes without complications (n = 12).The demographic characteristics and baseline laboratory findings of the study population presented in Tables 1 and 2. Admission systolic and diastolic blood pressure was 115/70 mmHg. Total diuretic dose was 151.43 ± 33.97 mg. Average EF was 23.5% ± 8.7% and mean ProBNP was 6343.76 pg/mL in our study population. Current medications for heart failure patients presented in Table 3. Changes in depression score of HF patients before and after dopamine treatment was showed significantly (before value: 18.95 ± 9.89; after

Table 3. Current medications for heart failure patients

Group of drugs	Data n (%
Diuretics	40 (71.4)
Furosemide	30 (71.4)
Spironolactone	16 (38.1)
Spiranolacton+Hydrochlorotiazid	4 (9.5)
ASA+Klopidogrel	24 (57.1)
Statin	8 (19)
ACEI	6 (14.3)
ARB	10 (23.8)
Beta-blocker	16 (38.1)
Digoxin	6 (14.3)
Nitrates	8 (19)
Warfarin	2 (4.8)
Ivabradine	4 (9.5)
Trimetazidine	12 (28.6)

ASA = acetylsalicylic acid, ACEI = angiotensin converting enzyme inhibitors, ARB = angiotensin receptor blockers

Table 4. Changes in parameters of HF patients before and after dopamine treatment

	Before	After	*P* value
Depression score	18.95 ± 9.89	17.29 ± 10.30	**< 0.001***
Systolic blood pressure (mmHg)	115 ± 20	117 ± 17	0.342
Diastolic blood pressure (mmHg)	70 ± 11	69 ± 10	0.279

Table 5. Comparison of parameters in groups that decreased and not changed depression score

Parameters	Decreased group (n = 32) Mean rank	Not changed group (n = 10) Mean rank	*p* value
Ages	22.63	17.90	0.286
ProBNP	23.00	16.70	0.156
BUN	18.75	30.30	**0.009**
Cr	20.31	25.30	0.261
NA	21.50	21.50	1.000
K	21.25	22.30	0.813
Hb	21.06	22.90	0.678
EF	18.88	29.90	**0.010***
LVEDD	18.88	29.90	0.311
LVESD	22.81	17.30	0.213
RAA	19.19	28.90	**0.027**
LAA	19.38	28.30	**0.043**
Total diuretic dose	21.81	20.50	0.758
SBP	19.31	28.50	**0.032**
DBP	19.69	27.30	0.071

EF = ejection fraction, LVEDD = left ventricle end-diastolic diameter, LVESD = left ventricle end-systolic diameter, LAA = left the atrial area, RAA = right atrial area, Hb = hemoglobin, BUN = blood urea nitrogen, Cr = creatinine, Na = sodium, K = potassium, CRP = C-reactive protein, SBP = systolic blood pressure, DBP = diastolic blood pressure

value: 17.29 ± 10.30, $p < 0.001$) however systolic and diastolic pressure was not significant (Table 4). Comparison of parameters in groups that decreased and not changed depression score presented in Table 5.

DISCUSSION

The results showed that low-dose dopamine associated with a significant reduction in depressive symptoms, and its anti-depressive effect influenced by EF and systolic blood pressure [8]. To our knowledge, this is the first trials to evaluate the effects of low-dose dopamine on symptoms of depression in HF patients in the hospital. Depression has been shown to be a risk factor for poor outcomes amongst heart disease patients. In a study of 1300 patients, 10.0% had a depression diagnosis in patients with cardiovascular disease [9]. Another study showed that enhanced depressive symptoms estimated long-term mortality in patients with heart failure [10]. In another famous trial, depression was found to be a powerful predictor of repeated hospitalizations for HF [11]. In the trial, depressed patients, by comparison, nondepressed, were hospitalized for HF 1.45 times more often, suggesting screening for depression early in the course of HF management. Patients with HF and depressive

symptoms commonly suffer from more reduced quality of life, declining functional status, more significant symptom burden, poorer adherence, more frequent rehospitalizations, and worse survival [12-14].

The effect of dopamine on depression is not known in heart failure patients. Dopamine is a catecholamine, and its effects are dose-dependent in patients with cardiogenic shock. At low doses (< 3 μg/kg/min), dopamine causes vasodilation in the body vasculature including the coronary and renal arteries [15]. Low-dose dopamine (< 5 μg/kg/min), widely combined with furosemide, is increased renal vasodilatation and blood flow, reduce the effects of norepinephrine and aldosterone, and promote natriuresis via effects on dopamine-1 and two receptors [16]. A critical study concluded that low-dose dopamine could worsen renal perfusion in patients with acute renal failure, supporting a trend to desert the routine use of low-dose dopamine in critically ill patients [17]. However, other studies challenge this conclusion. The Dopamine in Acute Decompensated Heart Failure (DADHF) Trial found that the combination of low-dose furosemide and low-dose dopamine is equally effective as high dose furosemide and associate with improved renal function and potassium homeostasis, as well [18].

Entry of dopamine into the brain is regulated by endothelial cells at the blood-brain barrier. Moreover, vascular smooth muscle contraction is controlled to a substantial degree by dopamine D1 receptors [19]. At dopamine treatment doses, dopamine binding to vasculature receptors is likely to result in vasodilation and local blood flow increases [20]. Thus, it is tempting to speculate that dopamine treatment leads to the development of microvascular changes such as angiogenesis, which under particular circumstances, can enhance the transport of the drug across the blood-brain barrier. Indeed, the autoradiographic data suggest that enhanced blood-brain barrier permeability, as well as concomitant increases in local cerebral blood flow, are dopamine-dependent phenomena that are not present in the off-state. We think that antidepressive effect can originate from these physiologic alterations. Physiological effects may be substantial mechanism into the explanation of antidepressive effect, in that depression has been linked to raised sympathetic activity, hypercoagulability, enhanced inflammation, endothelial dysfunction, and decreased heart rate variability, each of which has been associated with adverse clinical outcomes in patients with HF [21]. Additionally, all of the above factors may be improved significantly by the antidepressant effect of dopamine.

Limitations

Our trial has some limitations. Firstly, the patient population should be increased. An imaging method can be used to evaluate brain blood flow.

CONCLUSION

Low-dose dopamine treatment was associated with a demonstrable benefit in the symptoms of depression in clinically unstable HF patients. Large-scale, high-quality RCTs are needed to verify the benefits of exercise training in those populations. The evidence confirmed here should encourage physicians to recommend low-dose dopamine as a clinically substantial way to diminish the symptoms of depression in patients with HF.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

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